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RESUSCITATION OF THE ASPHYXIATED NEWBORN INFANT

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The initiation and maintenance of respiration in the asphyxiated newborn infant has always been of profound interest both to the obstetrician and to the pediatrician. As a consequence, the best means of achieving this purpose has been the subject of wide discussion.[1] Numerous methods have been advocated, none of which has been entirely satisfactory. Since it became accepted that the care of the newborn infant should be entrusted to the pediatrician, progress has been more satisfactory.

An attempt has been made to review methods which have been suggested from time to time and to incorporate the best of them into a routine which is sufficiently facile to apply to any type of asphyxia and yet does not demand such great technical skill that only an expert can carry it out. We think the result is one that may be easily understood and utilized.

In compiling such a routine, certain clinical factors that occur prenatally and during delivery, that either cause or contribute to the asphyxia of the child, have been taken into consideration. Our purpose in presenting this paper is to assemble these facts compactly in the hope of impressing those who come in contact with such circumstances with the importance of these various factors and the necessity of knowing

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1. Mathieu, A., and Holman, A.: Resuscitation of the Asphyxiated Newborn, J. A. M. A. **92**:1917-1918 (June 8) 1929. Henderson, Y.: The Prevention and Treatment of Asphyxia in the Newborn, ibid. **90**:583-586 (Feb. 25) 1928. Eastman, N. J.: Fetal Blood Studies: Chemical Nature of Asphyxia Neonatorum and Its Bearing on Certain Practical Problems, Bull. Johns Hopkins Hosp. **50**: 39-50 (Jan.) 1932. Henderson, Y.: Resuscitation, J. A. M. A. **103**:750 (Sept. 8); 834-837 (Sept. 15) 1934; Fundamentals of Asphyxia, ibid. **101**:261-266 (July 22) 1933. Flagg, P. J.: Resuscitation, Am. J. Surg. **34**:591-597 (Dec.) 1936. Coryllos, P. N.: Atelectasis, Asphyxia and Resuscitation in the Newborn: Anatomic, Physiologic, and Experimental Data, Am. J. Obst. & Gynec. **21**:512-525 (April) 1931.

how to handle the asphyxiated baby with skill and dispatch. Certainly it is as necessary for an obstetrician to know how to resuscitate a living child as it is for him to know how to deliver that child in a living state. The necessity is plain for the pediatrician, who must first handle that child, to be in full cognizance of the fact that a good start predisposes to an easier course throughout life.

Asphyxia has long been classified into two types: asphyxia pallida and asphyxia livida. This classification, however, is indefinite and vague and has not proved satisfactory. The classification suggested by Litchfield and Beilly [2] more clearly defines the types of asphyxia:

1. Mild asphyxia. The infant resists movements of the head and limbs. Mucous plugs and amniotic fluid fill the mouth and pharynx.

2. Moderate asphyxia. Muscle tonus is absent; there is no resistance to opening the mouth. No reflex irritation is induced by aspiration or by stimulation of the glottis.

3. Severe asphyxia. The infant does not respond to attempts at resuscitation. He appears livid or pallid. There is absence of any respiratory movements, and only an occasional flicker of the cardiac impulse may be detected through the thoracic wall. The upper respiratory tract has become a collapsed tube.

CAUSATION OF ASPHYXIA

There are certain conditions occurring during the prenatal period that have considerable effect on the causation of asphyxia. Outstanding are the various forms of toxemia of pregnancy: the preeclampsias, eclampsia, nephritis and marked hypertension. A mother who has one of these complications of pregnancy has a greater chance of delivering an asphyxiated infant than does a mother with an uncomplicated pregnancy. This is unquestionably due to the toxic effect on the respiratory mechanism of the child. Heart disease with congestive failure and severe anemia from any cause also predispose to delivery of infants who are weak and narcotized at birth. Other prenatal factors to be considered are any causes which may make the mother deliver her child prematurely.[3] Premature infants are notorious for their irregularities of respiratory effort, and there is considerably more resuscitatory effort necessary to initiate and maintain respiration in a premature infant than in a full term baby.

Prepartal Analgesia.—The discussion of prepartal analgesia is one which has filled many pages. Few physicians have identical methods; each has his own favorite drug. In the series of cases discussed in this

2. Litchfield, H. R., and Beilly, J. S.: Asphyxia of Newborn, M. Ann. District of Columbia **7**:307-313 (Oct.) 1938.

3. Breese, B. B., Jr.: Influence of Factors Before and at Time of Delivery on Premature Mortality, J. Pediat. **12**:648-663 (May) 1938.

paper, opportunity has been afforded us to observe the action of the following drugs, either singly or in combination: morphine sulfate, scopolamine hydrobromide, sodium amytal, sodium propylmethylcarbinylallylbarbiturate (seconal), pentobarbital sodium, barbital sodium (soluble barbital U. S. P.) and sodium amylbetabromallylbarbiturate (sigmodal). A detailed discussion of the effects on the respiration of the newborn infant seems appropriate. Morphine has long been known to be a respiratory depressant. Its use alone causes definite narcosis of the unborn infant in about thirty minutes after its administration to the mother. The influence lasts for four hours, reaching its maximum effect in two to two and a half hours after its administration. Babies delivered within four hours after its administration usually show the following symptoms: limpness, lividity and absence of reflexes. Breathing is initiated only after from ten to twenty minutes of resuscitative efforts, and even then respiration is maintained poorly. Cyanosis and cessation of breathing may occur as long as eight hours after delivery. These babies are slow in crying after birth, and they give a short, weak moan rather than a lusty cry. Eight to twelve hours are often necessary before the baby shows complete recovery from the influence of morphine. Babies delivered more than four hours after its administration generally escape any effects on the respiration.

Scopolamine given alone has a somewhat indefinite action on the baby.[4] Some infants delivered within four hours after its administration come under the classification referred to as moderately asphyxiated, but they can easily be made to breathe by minor efforts at resuscitation and have no difficulty in maintaining respiration. The effects from the combination of morphine and scopolamine, however, which is so often used, differ in detail but little from the previously described effects of morphine. When morphine or morphine and scopolamine are used with barbiturates, especially sodium amytal and seconal in combination or singly, little or no depressant effect is noted in addition to the results already discussed from administration of morphine alone. However, the use of morphine and pentobarbital sodium produces a marked respiratory depression which combines the worst features of each given alone.

Many barbiturates have been advocated for use in prepartal analgesia. Those which are most frequently used at Touro Infirmary, in New Orleans, are sodium amytal, seconal, pentobarbital sodium, sigmodal and barbital sodium. One sweeping statement may be made about these barbiturates, with one exception. With the exception of pentobarbital sodium, no ill effect has been observed from the use of any of the other barbiturates, regardlesss of dosage or time of administration.

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4. Irving, F. C.; Berman, S., and Nelson, H. B.: The Barbiturates and Other Hypnotics in Labor, Surg., Gynec. & Obst. **58**:1-11 (Jan.) 1934.

It has been especially noteworthy that in many spontaneous deliveries or in low forceps and episiotomy deliveries, after administration of large doses of barbiturates (especially sodium amytal alone or in combination with seconal), the baby is born pink, crying vigorously and breathing at once, with no subsequent cyanotic attacks.

However, the use of pentobarbital sodium, either by itself or in any combination, is dangerous and to be condemned. The use of as little as 1½ grains (0.09 Gm.) four to six hours prior to delivery has produced narcosis in the child. The effects of pentobarbital sodium begin to appear in the infant about thirty to forty-five minutes after the drug is taken by the mother, and they are long lasting, still being present six to eight hours after ingestion; the effects reach their height about two hours after ingestion and remain at a maximum for the next two hours. The infant born under the effects of pentobarbital sodium presents such a characteristic appearance that an observer familiar with the appearance may realize merely by looking at the baby that pentobarbital sodium has been given to the mother. The baby is a deep purple, limp, with absolutely no reflexes; he breathes with difficulty only after from ten to thirty minutes of intensive resuscitative efforts and then fails to maintain respiration well, repeated resuscitations being necessary before a regular rate of respiratory rhythm is established. The baby has several cyanotic attacks and cessations of respiration during the first twelve hours of life and needs close and careful attention, fails to cry at all for the first eight to twelve hours of life and is indifferent to all sorts of stimuli for twenty-four hours after birth. Even after respiration is well established, the purple color lingers on the hands and feet for from twelve to twenty-four hours; the heart rate is rapid and the pulse is shallow; circulation appears to be poorly established.

The foregoing observations seem fully to justify the assertion that the use of pentobarbital sodium should be discontinued and that morphine should not be administered if delivery is possible within four hours. Greater reliance should be placed on the relatively harmless barbiturates.

Prepartal Anesthesia.—The effects of such anesthetics as cyclopropane, ethylene and ether have been observed; the last has often been used after induction of anesthesia by either of the former two.[5] In some cases, ether has been the only anesthetic used; in others, after anesthesia by ethylene or cyclopropane had been contemplated, ether has been resorted to for greater relaxation. When cyclopropane or ethylene is used alone, little or no narcosis is observed; but when ether

5. Rosenfeld, M., and Snyder, F. F.: The Factor of Anesthesia in the Pathogenesis of Asphyxia Neonatorum, Am. J. Obst. & Gynec. **38**:424-430 (Sept.) 1939.

is used, narcosis is frequently seen. The extent of this narcosis depends on the length of time ether is used and the depth of anesthesia produced. When narcosis has followed the use of ether, only moderate asphyxia has been noted, which responded to a short period of resuscitative efforts. It is frequently difficult to initiate respiration after ether narcosis, but once begun, it is maintained without further trouble. The effects of ether on the infant may be exemplified by the observations made on a baby delivered by cesarean section after anesthesia had been induced by ethylene and continued by ether. Because of certain surgical difficulties, the mother was in the state of surgical anesthesia for over an hour before the baby could be delivered. When placed on the resuscitation table, the baby literally reeked of ether; and when the intratracheal catheter was introduced into the trachea, the characteristic bitter taste of ether was readily discernible. Ten minutes were necessary to institute respiration. The baby then cried lustily, and the subsequent course was barren of further troubles.

Type of Delivery.—The type of delivery plays a most important role in the immediate causation of asphyxia. Primiparas present far more infants with asphyxia than do multiparas. Deliveries in which trauma is great result in a high proportion of moderately and severely asphyxiated infants. If all the other previously discussed factors are eliminated, spontaneous deliveries, deliveries by low forceps or by low forceps and episiotomy seldom produce infants for whom resuscitation is necessary. Of course, this statement does not refer to premature infants. Deliveries by version and extraction, breech extraction and mid forceps result in a great number of asphyxiated infants. Trauma during delivery is apparently a potent factor, because when it occurs the babies are more severely asphyxiated and demand greater resuscitative effort. It must be remembered that the factors which retard labor or cause an abnormal type of delivery will also contribute to causing asphyxia. In these types of deliveries, anesthesia necessarily must be of greater duration and depth than in the less complicated deliveries.

Cesarean section is in a different category from the previously discussed types of delivery. Whatever factor initiates spontaneous respiration in an infant, it is certainly present to a greater degree in babies delivered by the usual birth channel than in those delivered by cesarean section, a fact which in itself predisposes to some asphyxia. Fifty-four of our 196 infants were delivered by cesarean section, and in all of them some degree of asphyxia was present: in 10, the mild type; in 40, the moderate type; and in 4, the severe type, in each instance complicated by severe anemia caused by premature separation of the placenta. Considerable benefit has been noticed from routine intratracheal catheterization, regardless of the degree of asphyxia. By this procedure we remove from 1 to 10 cc. of blood, mucus and amniotic fluid from the upper

respiratory tract of these infants, whereas in children delivered through the parturient canal there is often no material to be removed and it rarely reaches 2 cc. in amount.[6]

Type of Labor.—The type of labor also plays its part in asphyxiation. Prolonged labor in which considerable force is exerted and progress is slow is notorious for its ill effect on the baby. The effect from premature separation of the placenta with resultant poor oxygenation of the blood explains itself. Similar effects may be attributed to a bleeding placenta praevia, to prolapse of the cord and to kinking, knotting or compression of the cord by some hard part of the infant or of the maternal pelvis.

METHODS OF RESUSCITATION

In this study, the following methods have been considered:

(*a*) The use of alternating immersions in hot and cold water.
(*b*) Swinging the child between the legs of the resuscitator, with head down.
(*c*) Folding the child in "accordion" fashion.
(*d*) Manual manipulation of the chest by alternately compressing and releasing the thoracic cage.
(*e*) Mouth to mouth insufflation of the lungs.
(*f*) Intratracheal catheterization with aspiration of the trachea and upper bronchi.
(*g*) Intratracheal catheterization with the use of a mechanical apparatus to insufflate the lungs with a mixture of carbon dioxide and oxygen under visual pressure.
(*h*) The use of a baby laryngoscope and intratracheal catheterization under direct visualization.
(*i*) Stripping mucus from the throat by hanging the baby head downward and stroking the neck from chest to chin.
(*j*) Spanking the child, snapping the soles or rubbing the skin with towels.
(*k*) Sprinkling cold water or ether on the skin.
(*l*) Aspiration of the nose, mouth and throat with a rubber bulb syringe.
(*m*) Intravenous, subcutaneous and intramuscular use of such drugs as alpha lobeline, caffeine with sodium benzoate, coramine (a 25 per cent solution of pyridine beta carbonic acid diethylamine), metrazol, epinephrine and strychnine.
(*n*) The application of carbon dioxide and oxygen or plain oxygen by face mask.
(*o*) Use of mechanical apparatus, such as the Drinker respirator and the Easton and Johnson resuscitator.

Every consideration has been given to the fact that direct insufflation of the lungs with the gases mentioned not only is a powerful stimulation

6. Since these observations on the various factors influencing neonatal asphyxia have been made by us, a contribution to the study has been published by W. C. C. Cole, D. C. Kimball and L. E. Daniels (Etiologic Factors in Neonatal Asphyxia, J. A. M. A. **113**:2038-2046 [Dec. 2] 1939). Their conclusions run a strikingly parallel course to ours, which were reached without knowledge of their work.

of reflexes but affords aid to the child until spontaneous respiration begins. It is constantly borne in mind that the infant is a most delicate organism and that any resuscitative method that is in any way violent or traumatic or involves much handling of the child must automatically be ruled out of consideration.

Twelve hundred newborn infants have been studied, resuscitation having been necessary for 196. No infant has been included in the 196 who breathed spontaneously and maintained respiration thereafter. Only

The pediatrician stands ready to receive the baby when the necessity of resuscitation is anticipated. The table on which resuscitation is performed is fully equipped with everything which may be needed, and the Easton and Johnson resuscitator next to it is ready for immediate use.

those who could be classified as having one of the three types of definite asphyxia mentioned previously have been included. A pediatrician, especially qualified in methods of resuscitation, has been at hand for the delivery of any infant who might need resuscitation. The criteria for his services have been: delivery by mid or high forceps, cesarean section, version and extraction or breech extraction; a fetal heart rate above 160 or below 100; toxicity of the mother; premature separation

of the placenta; prolapse of the cord; bleeding placenta praevia; premature delivery, and administration of morphine or pentobarbital sodium.

The routine adopted for handling infants for whom the necessity of resuscitation is anticipated is as follows: In order adequately to meet any emergency in which resuscitation is demanded, a table 3 feet (91 cm.) wide and 4 feet (122 cm.) long, with a 4 inch (10 cm.) protective border around the edges, is provided. This table is covered with a sterile sheet on which is placed a warmed blanket. The table is then prepared by laying out sterile towels, an intratracheal catheter with a glass saliva trap, hypodermic syringes containing $\frac{1}{20}$ grain (3 mg.) of alpha lobeline and 15 minims (0.92 cc.) of coramine, scissors, cord clamps and cord dressings. By the side of the table is an Easton and Johnson resuscitator which is checked daily, both as to the contents of the gas tanks and as to the efficiency of the mechanical apparatus. The pediatrician, fitted with sterile gown, mask and gloves, stands ready to receive the baby. Many obstetricians are in favor of aspirating the mouth and nostrils of the infant with a rubber bulb syringe as soon as the baby is born. This procedure aids slightly, but it is preferred that time not be taken for it that could better be used to deliver the baby sooner into the attendant pediatrician's hands.

After the cord is cut, the baby is received by the pediatrician in a sterile towel and placed on the table. He is immediately wrapped in the warm cover, and the skin is gently, rapidly rubbed for a few seconds. The fingers of the pediatrician's left hand are placed beneath the neck of the child and the head hyperextended. With the intratracheal catheter, the nostrils, mouth, pharynx and nasopharynx are immediately aspirated of mucus, amniotic fluid, blood or meconium. These three stimuli (warmth, cutaneous friction and aspiration of the upper respiratory tract) are usually sufficient to institute respiration in those infants who are but mildly asphyxiated. If respiration does start, plain oxygen by face mask is administered for several minutes until the respirations are regular in volume and rate or until the baby cries. In case respiration does not start, alpha lobeline is at once administered via the umbilical vein, and the intratracheal catheter is introduced into the trachea. This is done by withdrawing the left hand from beneath the neck and placing the left index finger in the mouth until the tracheal opening is felt beneath the tip of the finger. The catheter is introduced with the right hand and run along the side of the finger until the tip is reached, and then the end of the catheter is diverted beneath the tip of the finger and into the tracheal meatus. Gentle aspiration is performed until the trachea and upper bronchi are clear, and then by means of the pediatrician's own breath from five to ten gentle inspirations and expirations are made, while the thoracic wall is watched closely for the amount of expansion. Quite often the limp pharynx begins to tighten and show

some muscle tone, which is a definite indication that respiration will soon start. If respiration has started, as is usual in the moderately asphyxiated infant, oxygen is again administered by face mask until the respiration is normal in volume and rate or until the baby cries. In the case of the more severely asphyxiated infant, when respiration will not start, the catheter is withdrawn, the head again hyperextended and the face mask of the Easton and Johnson resuscitator adjusted over the face. The necessity of having the mouth opened wide as long as the face mask is in place cannot be too strongly emphasized. It is believed that most failures with this apparatus are due to the fact that the baby's mouth is not opened wide. The alternate pressure and suction mechanism is started, plain oxygen being used at first, at a rate of 30 to 36 cycles per minute. Coramine in doses of 2 minims (0.12 cc.) is administered subcutaneously at ten minute intervals until respiration is established; 2 minims of epinephrine is given subcutaneously if the beat of the heart flags. This method of resuscitation is used continuously until spontaneous respiration is attempted by the infant at a rate of at least eight to ten respirations per minute. At this time, the pressure suction apparatus is switched to that of the continuous flow of oxygen at a pressure of 13 mm. of mercury, and 5 per cent carbon dioxide and 95 per cent oxygen is substituted for oxygen alone. If respiration continues and becomes regular, the administration of coramine is stopped, the face mask is removed and the baby is watched closely for any irregularities of respiration. The administration of oxygen should be resumed immediately if any suspicious sign of irregular breathing is observed. If, while oxygen is being administered continuously, spontaneous respiration ceases, the mechanism is once again switched on until spontaneous efforts to breathe are resumed. If after two to three hours of these procedures the heart still beats but no attempts at respiration have been made, the baby is placed in a small Drinker respirator with an oxygen tent over his head. If the baby's heart stops beating, no harm can be done and occasional benefit may be derived by the use of epinephrine intracardially.

AFTER-CARE

The immediate after-care, once respiration is established normally, is of great importance. All moderately or severely asphyxiated infants are placed in an incubator or warmed crib under an oxygen tent for at least twelve hours or longer if necessary. Careful frequent observations should be made to detect irregularity of the respiration. A dose of 2 minims of coramine is given every two hours for four to six doses; insufflations of carbon dioxide and oxygen by face mask for two or three minutes are given for twelve hours at two hour intervals; orders are left for immediate use of epinephrine, coramine or the pressure suction apparatus of the Easton and Johnson resuscitator if cessation of respiration should occur. Intratracheal catheters are used to aspirate

mucus from the upper respiratory tract if necessary, but the trachea should not be entered unless respiration stops. It is often advisable to pass a stomach tube and empty the stomach, for often a considerable amount of mucus and amniotic fluid has been swallowed and may be regurgitated into the upper respiratory tract.

ADVANTAGES OF SUGGESTED ROUTINE

The following advantages may be claimed for our routine:

1. Immediate warmth.
2. Gentle, absolutely minimum handling of the infant.
3. Immediate oxygenation of the blood stream, preventing anoxemia to the brain and damage to the respiratory center; stimulation to this center by oxygenation.
4. Maintenance of heart action by the bellow action of the lungs.
5. Sufficient simplicity of methods, so that any one can be rapidly trained to handle an asphyxiated infant adequately.
6. Methods and equipment to permit skilful handling of any type of asphyxia that presents itself.
7. Ability to maintain artificial respiratory movements for long periods without damage to the baby.

DATA FOR 196 NEWBORN INFANTS WITH ASPHYXIA

The data for the 196 newborn infants may be tabulated briefly as follows:

1. Type of asphyxia:

Mild	80
Moderate	89
Severe	27
Total	196

2. Results of efforts:

Unable to start respiration	1
Respiration maintained less than 1 hour	1
Respiration maintained longer than 1 hour, but less than 2 hours	4
Respiration maintained longer than 24 hours	190
Total	196

3. Length of time necessary to initiate respiration:

Less than 5 minutes	76
5 to 10 minutes	46
10 to 15 minutes	31
15 to 30 minutes	18
30 to 60 minutes	10
1 to 2 hours	9
2 to 3 hours	1
3 to 4 hours	4
4 to 5 hours	1
Total	196

4. Deaths:

Infants with mild asphyxiation	0
Infants with moderate asphyxiation	1
Infants with severe asphyxiation	7
Total	8

5. Causes of death:

Intracranial hemorrhage	3
Atelectasis	3
Prematurity	2
Total	8

EFFECT OF DRUGS USED TO RELIEVE ASPHYXIA

For the purpose of determining the value of various drugs, the following observations were made:

Drug	Subcutaneous Administration	Intravenous Administration
Physiologic solution of sodium chloride	No results	No results
Alpha lobeline 1/20 grain (3 mg.)	No results	Immediate response of 2 or 3 deep respirations, often the cause of initiating respiration; no tendency toward maintaining respiration
Coramine 2 to 6 minims (0.12 to 0.37 cc.)	Increases pulse rate slowly; aids in maintenance of respiration	No immediate response; tends to maintain respiration after it is started; supports heart action
Metrazol 2 to 6 minims	Increases pulse rate rapidly; aids in maintaining respiration	Occasional immediate response of 1 or 2 deep initial respirations, but this is not constant; tends to maintain respiration after it is started; aids heart action
Epinephrine (1:1,000) 2 to 6 minims	Increases pulse rate rapidly; no effect on respiration	No respiratory response; greatly supports heart action
Puncture with hypodermic needle	No results	No results

Alpha lobeline given intravenously is of value in starting respiration, and coramine given subcutaneously perpetuates respiration once it is started. Epinephrine is used only when there is need for a powerful heart stimulant.

COMMENT

All of the foregoing data pertain to resuscitation in a modernly equipped hospital. The occasional resuscitation necessary in the poorly equipped home must also be considered. From our results, it is believed that practically any child can be revived by the use of the intratracheal catheter and alternate inspiration and expiration through the catheter by the pediatrician. Intratracheal catheterization is a most valuable adjunct to the practice of obstetrics or pediatrics and should be included in the armamentarium of practical facts taught to every graduating medical student who might possibly ever come in contact with an asphyxiated newborn infant. This one procedure alone, easily learned after two or three demonstrations, should save most of the babies that would otherwise die from asphyxia.

SUMMARY AND CONCLUSIONS

A detailed method of resuscitation of asphyxiated infants is presented. The method is rapidly and easily learned, requires no great technical skill and is productive of most satisfactory results.

Prepartal factors and conditions arising at the time of delivery that might cause asphyxia in the infant are discussed.

The use of morphine four hours before delivery and the use of pentobarbital sodium six hours prior to delivery are not advisable. Greater reliance may be placed on other barbiturates, such as sodium amytal, seconal, sigmodal and barbital sodium. While ether does cause some definite narcosis in the child, it is a narcosis easily overcome.

The use of alpha lobeline via the umbilical vein to aid in the institution of respiration is advised, with the use of either coramine or metrazol subcutaneously as a respiratory and circulatory aid thereafter.

The use of the intratracheal catheter should be stressed.

Dr. Walter Levy and Dr. Arthur Caire Jr. provided case material.

EPIPHYSIAL DYSGENESIS ASSOCIATED WITH HYPOTHYROIDISM

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Clinical reports of the abnormalities of epiphysial ossification which occur in hypothyroidism during childhood have been recorded in the Swiss or German literature by Läwen [1] in 1909 (1 case), Roth [2] in 1918 (3 cases), von Seemen [3] in 1928 (2 cases) and Looser [4] in 1929. Von Seemen called the condition "osteochondropathia cretinoidea." Looser described the abnormal structure of the epiphyses in 20 of 30 cretins whom he examined in Switzerland. In 1927 Fairbank,[5] in England, reported instances of dwarfism with "stippled epiphyses" but failed to recognize the thyroid disturbance. There are few reports in the American literature. Brailsford,[6] in 1935, mentioned 1 case in a monograph on radiology. Cavanaugh, Shelton and Sutherland,[7] in 1936, reported 5 cases of osteochondritis of the capital femoral epiphyses which they considered due to hypothyroidism. However, in all their cases the

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1. Läwen, A.: Zur Kenntnis der Wachstumsstörungen am Kretinenskelett, Deutsche Ztschr. f. Chir. **101**:454, 1909.

2. Roth, O.: Berichte der Gesellschaft der Aerzte des Kantons Zürich, Cor.-Bl. f. schweiz. Aerzte **48**:951, 1918.

3. von Seemen, H.: Osteochondropathia cretinoidea, Arch. f. klin. Chir. **152**: 616, 1928.

4. Looser, E.: Die Kretinenhüfte, Schweiz. med. Wchnschr. **10**:1258, 1929; Ueber die Ossifikationsstörungen bei Kretinismus, Verhandl. d. deutsch. path. Gesellsch. **24**:352, 1929.

5. Fairbank, H. A. T.: Some General Diseases of the Skeleton, Brit. J. Surg. **15**:120, 1927.

6. Brailsford, J. F.: The Radiology of Bones and Joints, ed. 2, Baltimore, William Wood & Company, 1935, p. 214.

7. Cavanaugh, L. A.; Shelton, E. K., and Sutherland, R.: Metabolic Studies in Osteochondritis of the Capital Femoral Epiphysis, J. Bone & Joint Surg. **18**:957, 1936.

condition was unilateral, dysgenesis was not found in other epiphyses and the existence of hypothyroidism is open to doubt. Reilly and Smyth,[8] in 1937, reported 5 undoubted cases and applied the term "cretinoid epiphyseal dysgenesis." Albright [9] reported 1 case in 1938, and Benjamin and Miller [10] described 3 similar cases. They also reported on a cretinoid boy with a slipped femoral epiphysis on one side whose roentgenograms did not show the characteristic abnormalities of the epiphyses. In most reports in the literature the disturbance is described only in the head of the femur. However, Reilly and Smyth found epiphysial dysgenesis in both ends of the humerus, ulna, radius, tibia, and fibula and in the vertebral column. None of the writers has attempted to correlate the distribution of the epiphyses involved with the age at which hypothyroidism occurs. Although it has been pointed out that thyroid treatment causes the abnormality to disappear, no mention has been made of the occurrence of the lesion in new centers of ossification which appear during treatment. However, in an article by Nobel and Kornfeld [11] reporting the treatment of a cretin with thyroxin there are excellent illustrations which show the appearance under treatment of new centers of ossification with characteristic stippling and multiple foci of ossification.

ROENTGENOGRAPHIC APPEARANCE OF VARIOUS STAGES OF EPIPHYSIAL DYSGENESIS

In studies of hypothyroid children, my attention was attracted first in certain long untreated patients by the spectacular abnormalities of ossification [11a] in the larger centers such as the head of the femur, the head of the humerus and the navicular bone of the foot. These were the lesions well described in the literature. Later, I found that after thyroid treatment was begun the new centers of ossification which appeared on the roentgenograms showed the same type of abnormality in one form or another. By means of serial roentgenograms taken at frequent

8. Reilly, W. A., and Smyth, F. S.: Cretinoid Epiphyseal Dysgenesis, J. Pediat. **11**:786, 1937.

9. Albright, F.: Changes Simulating Legg-Perthes Disease (Osteochondritis Deformans Juvenilis) Due to Juvenile Myxoedema, J. Bone & Joint Surg. **20**:764, 1938.

10. Benjamin, B., and Miller, P. R.: Hypothyroidism as a Cause of Disease of the Hip, Am. J. Dis. Child. **55**:1189 (June) 1938.

11. Nobel, E., and Kornfeld, W.: Beitrag zur Thyroxinbehandlung des kongenitalen Myxödems, Ztschr. f. Kinderh. **48**:216, 1929.

11a. In this paper the term "ossification" is used to describe the appearance of calcium in the roentgenogram of a cartilage. It does not necessarily imply that true bone is formed.

intervals, I was able to follow the evolution of the process of ossification from the time that calcification first appeared. This has enabled me to explain the reason for marked variations in structure that are found.

Under normal conditions ossification of an epiphysial cartilage, such as the head of the femur, appears in the roentgenogram as a single small area near the center of the cartilage. This grows outward toward the margins of the cartilage, assuming gradually the shape of the mature epiphysial end of the bone. The structure of the growing osseous center is fairly uniform and shows an orderly arrangement of trabeculae. When hypothyroidism exists during the period when extensive ossification of the cartilage would ordinarily take place, this normal course of ossification does not occur. Months or years may elapse after the normal time for the appearance of the center before any sign of ossification is made visible in the roentgenogram by the presence of calcium. Eventually, either without treatment or through thyroid therapy, the presence of calcification becomes apparent in the roentgenograms. However, instead of a single small center, there appear simultaneously multiple, small, irregular islets of calcification. These may be scattered over an area of considerable size, and this area is often broad, flattened and misshapen as compared with the normal mature epiphysis. As these multiple irregular islets grow larger or new ones appear, they begin to coalesce. There then appears to be a single center of ossification, which gives the impression of having undergone fragmentation because of irregular separations between the foci. With further growth and coalescence, there is formed a single large center of ossification which is irregular in shape and consistency. The margins are irregular, poorly defined and fluffy, and the whole mass has a spongy, porous, stippled or fluffy appearance. This is due to irregularities in the calcium deposits, which seem to be arranged in swirls and clumps instead of orderly trabeculae. Finally, there is a transition from the stippled or porous, irregular epiphysis to one of normal shape and structure. I shall show later that this transition occurs slowly without treatment but rapidly under treatment.

In figure 1, *A, B* and *C* show stages in the ossification of the head of the femur of a hypothyroid patient under treatment. In this patient no calcification was visible before treatment was started, and the first photograph shows the earliest stage of calcification. *D, E* and *F* illustrate the development of the head of the femur in another child, in whom ossification had begun before treatment. In untreated, as well as treated, patients with hypothyroidism I have encountered the process of ossification in the various stages which are illustrated here. Figures 2, 3, 4 and 5 illustrate the different stages of ossification in various cartilaginous centers.

OCCURRENCE OF EPIPHYSIAL DYSGENESIS DURING THYROID TREATMENT

The restitution of normal epiphysial structure by thyroid treatment has been previously described, but it has not been mentioned that an

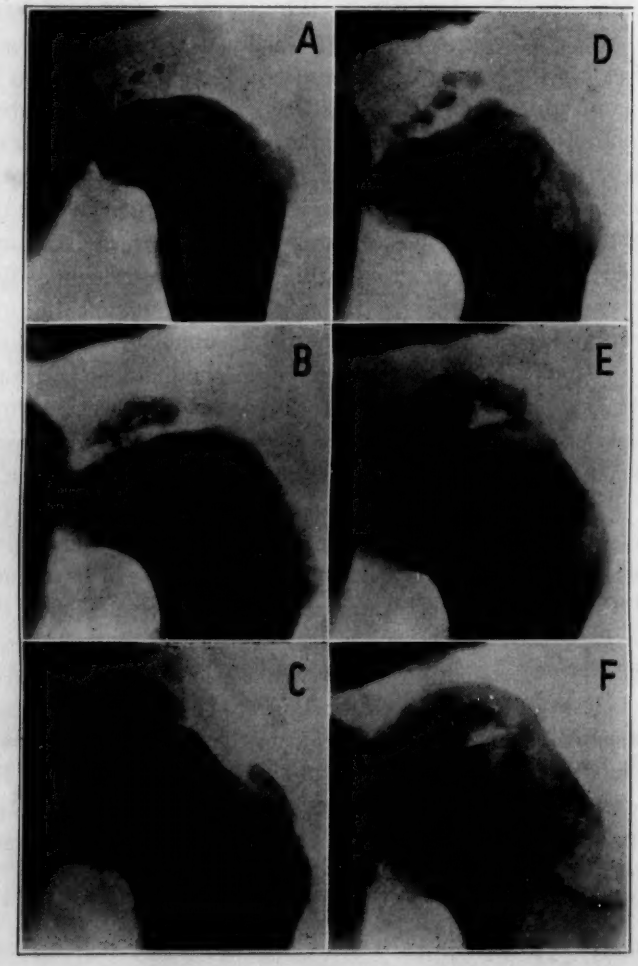

Fig. 1.—Development of head of femur in 2 hypothyroid children under thyroid treatment, which was instituted at 6 years and 8 years 9 months of age, respectively. *A* (case 13), first appearance of ossification two and a half months; *B*, five and a half months, and *C*, twenty-two months, after treatment was begun. *D* (case 15), before treatment; *E*, seven and three-fourths months, and *F*, twelve months, after treatment was begun.

epiphysis may ossify abnormally under treatment. I have repeatedly observed in serial roentgenograms that after thyroid treatment is begun

the new centers of ossification which first appear show the characteristic abnormalities which I have described, while centers developing later are normal. The course of ossification in 2 patients exhibiting this phenomenon to a marked degree is outlined in table 1. Following are notes concerning the roentgenographic appearance of the centers of ossification in the first of these patients.

CASE 13.—*Hypothyroid dwarf, previously untreated.*

On Dec. 11, 1937, the patient's chronologic age was 5 years 10 months, the age judged by height 15 months and the osseous age 5 months. The cuboid bone was normal. The distal epiphysis of the femur and the proximal epiphysis of the tibia were of about the size normally found at birth and were normal in structure. The head of the humerus was small and irregular, and had multiple foci of calcification. The centers of ossification of the carpus, the head of the femur and of all other bones were absent. Thyroid treatment was begun December 15.

By February 28, 1938, two and a half months after treatment was begun, the femoral and tibial centers of ossification at the knee had grown larger, irregular and fluffy at the periphery. The head of the humerus had grown larger and was spongy. The greater tuberosity of the humerus had appeared and was spongy. Ossification of the head of the femur was just appearing as small, widely separated islets of ossification scattered over a large area (*A*, fig. 1). Ossification of the distal epiphyses of the radius (*A*, fig. 2), the tibia and the fibula (*C*, fig. 3) had appeared as multiple irregular foci, which were coalescing. The capitellum had several small irregular centers of ossification. The centers of ossification which normally appear during the third year were still absent.

By May 27, five and a half months after beginning treatment, the centers of ossification at the knee and shoulder were less irregular. The islets of ossification of the head of the femur had enlarged and were coalescing to form an irregular stippled mass (*B*, fig. 1). Ossification of the distal epiphyses of the radius, the tibia and the fibula (*D*, fig. 3) appeared as single centers of ossification; these structures were assuming their normal shapes but had a slightly porous consistency. The new centers of ossification which had appeared were in the epiphyses of the metacarpal bones and the phalanges and the first cuneiform bone of the foot (*D*, fig. 3). Ossification was proceeding in these sites from multiple isolated foci.

By September 28, nine and a half months after treatment was begun, the head of the femur had a broad, flattened, mushroom shape, irregular outline and fluffy appearance. All the other centers of ossification which were shown in previous roentgenograms had assumed normal shape and structure except those of the cuneiform bones of the foot, which still showed multiple foci. Two new centers had appeared: in the navicular bone, which appeared to have multiple foci of calcification, and in the proximal epiphysis of the fibula, which was apparently normal.

On March 29, 1939, fifteen and a half months after treatment was begun, the head of the femur was still irregular and flattened, with a fluffy, fragmented appearance. The greater trochanter was now ossifying as an irregular fluffy mass. Ossification had appeared in the patella as a pinhead-sized center. All the other centers of ossification which had appeared previously had assumed normal shape and structure.

By November 11, twenty-two months after treatment was begun, the head of the femur was rounding into normal shape but was still flattened. The structure

TABLE 1.—*Occurrence of Epiphysial Dysgenesis During Thyroid Treatment**

Case	Date	Age Yr.	Age Mo.	Osseous Age, Yr.	Duration of Treatment, Mo.	Birth: Distal Epiphysis of Proximal Epiphysis of Tibia	3-5 Mo.: Head of Humerus	4-6 Mo.: Capitate and Hamate Bones	9-12 Mo.: Head of Femur	1 Yr.: Distal Epiphysis of Radius	1 Yr.: Distal Epiphysis of Tibia	2 Yr.: Capitellum	2 Yr.: Greater Tuberosity of Humerus	2 Yr.: Distal Epiphysis of Fibula	3 Yr.: Metacarpal Bones Phalanges of Hand	3 Yr.: Cuneiform Bones of Foot	3 Yr.: Triquetrum	4 Yr.: Navicular Bone	4 Yr.: Greater Trochanter	4 Yr.: Proximal Epiphysis of Fibula	5 Yr.: Patella	5-6 Yr.: Trapezium
13	12/11/37	5	10	½	0	N?	+	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O
	12/15/37	Treatment begun																				
	2/28/38	6		2	2½	N?	+++	N	+++	+++	+++	+++	+++	+++	O	O	O	O	O	O	O	O
	5/27/38	6	3	3	5½	N?	±	N	+++	±	N	±	±	N	+++	+++	O	O	O	O	O	O
	9/28/38	6	7	3¾	9½	N	N	N	++	N	N	N	N	N	N	±	N	N?	O	N	O	O
	3/29/39	7	1	4½	15½	N	N	N	+	N	N	N	N	N	N	N	N	N	+	N	±	O
	11/11/39	7	9	5½	22	N	N	N	±	N	N	N	N	N	N	N	N	N	±	N	+	N
15	1/ 4/38	8	9	2	0	N	+++	±	+++	±	+	±	++	±	O	O	O	O	O	O	O	O
	3/ 1/38	8	11	Treatment begun																		
	4/29/38	9		2	2	N	+	N	+++	++	++	±	+++	+	O	O	O	O	O	O	O	O
	6/14/38	9	2	3½	3½	+	+	N	++	+	++	±	+++	+	+++	O	+	O	±	++	O	O
	10/25/38	9	6	4	8	O	N	N	+	N	N	N	++	N	N	±	N	++	±	O	O	O
	3/ 3/39	9	11	5½	12	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	+	+

* O indicates that ossification has not occurred; N denotes a center of ossification showing normal structure, and +, abnormal ossification characteristic of epiphysial dysgenesis.

was more uniform and normal but still showed irregularities (*C*, fig. 1). The greater trochanter was irregular but more uniform in structure. The patella had grown larger and was irregular and granular. All the other centers were normal in structure. The trapezium and trapezoid had appeared, and the osseous age was between 5 and 6 years. The child was 39 inches (99 cm.) tall and had an age according to height of 3¾ years.

The data in table 1 serve to illustrate the following sequence of events, which has been found in many hypothyroid children who have been closely followed. When roentgenograms are taken before treat-

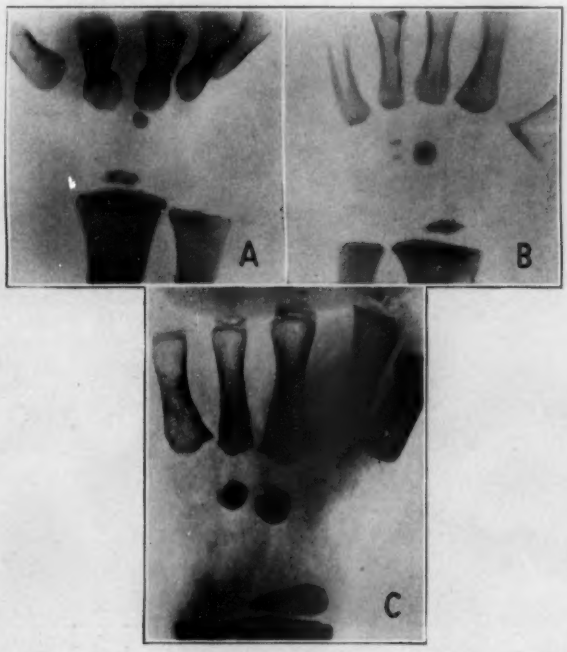

Fig. 2.—Dysgenesis of bones of hand. *A* (case 13), in hypothyroid dwarf aged 6 years, two and a half months after treatment was begun; epiphysis of radius shows stippling. *B* (case 12), in cretin aged 5 years, three months after treatment was begun; epiphysis of radius is stippled and hamate bone shows multiple centers of ossification. *C* (case 15), in hypothyroid dwarf aged 9 years, three and a half months after treatment was begun; triquetrum and epiphyses of metacarpal bones show multiple centers of ossification.

ment, many centers of ossification which normally should have appeared are absent, and most of those structures which are ossified show epiphysial dysgenesis. Treatment with thyroid brings about rapid ossification in those sites where it is overdue. If the earliest appearance of such centers of ossification is detected in the roentgenograms, the characteristic dysgenesis is observed. With further treatment, the parts in which

ossification first appeared rapidly assume normal structure, and at the same time new centers showing dysgenesis appear. Thus, under treatment, restitution of normal structure in parts where ossification is already present and abnormal ossification of new centers go on simultaneously. In roentgenograms taken at the same time, various stages of the process of ossification may be observed in different cartilages. Under treatment, the entire cycle, from the first appearance of multiple centers of ossification to the formation of a normally formed epiphysis, occurs rapidly, often in the course of a few months. The changes take

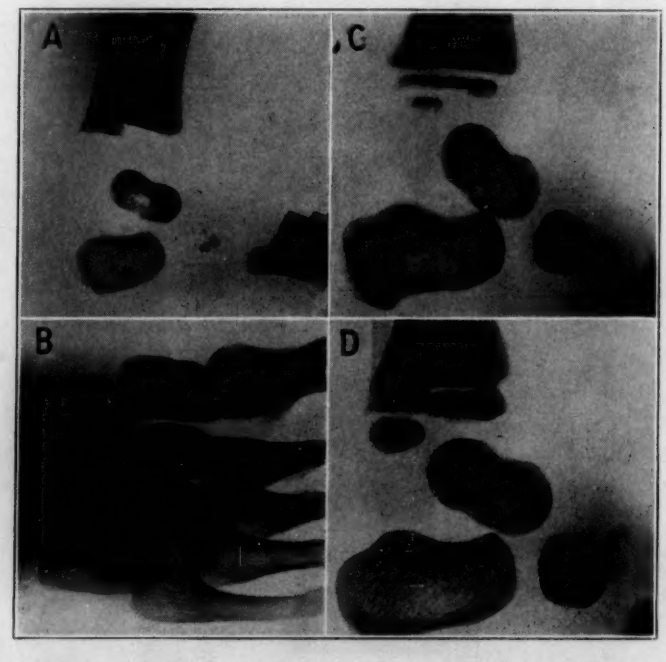

Fig. 3.—Dysgenesis of bones of tarsus and ankle. *A* (case 1), in untreated cretin aged 7½ months; cuboid bone shows multiple foci of ossification. *B* (case 17), in hypothyroid dwarf aged 12 years; thyroid deficiency had its onset at 3 years of age; navicular bone has fragmented appearance. *C* (case 13), in patient aged 6 years, two and a half months after treatment was begun; epiphyses of tibia and fibula are ossifying from multiple foci. *D* (case 13), five and a half months after treatment was begun, epiphyses of tibia and fibula are now well formed and the cuneiform bone is ossifying from multiple foci.

place more rapidly in some of the small structures, such as the carpal bones and the epiphyses of the metacarpal bones, than in larger ones, such as the head of the femur. Unless roentgenograms are taken at frequent intervals, the abnormal formation of many of the centers may not be observed. The most spectacular changes are usually found within two to six months after beginning of treatment.

DATA ON PATIENTS WITH HYPOTHYROIDISM

After becoming familiar with the various appearances which epiphysial dysgenesis presents, I reviewed serial roentgenograms of 25 children with hypothyroidism (table 2) and discovered evidences of the abnormality in many of the smaller structures which previously had not attracted my attention. In 22 instances roentgenograms had been taken before treatment was begun. In 16 of these (cases 1 to 16) hypothyroidism was either congenital or had developed within the first year of life, while in 6 (cases 17 to 22) the history suggested that it had developed later in childhood. I have included in the series 3 other children, 13 or 14 years of age (cases 23, 24 and 25), who had not had roentgenograms taken before treatment was begun, but therapy had been inadequate and intermittent and symptoms of hypothyroidism were still present.

It is seen in table 2 that characteristic abnormalities in one or more epiphyses were found in all but 2 of the 22 patients studied both before and during treatment and in the 3 patients who were inadequately treated before coming under observation. In the 2 patients (cases 7 and 8) in which epiphysial dysgenesis was not found, fourteen months and two years, respectively, had been allowed to elapse after the beginning of treatment before the roentgen examination was repeated. In the interval many new centers had appeared and had already reached a fairly advanced stage of development.

In order to correlate the distribution of the epiphyses involved with the span of life during which hypothyroidism remained untreated, in table 2 I have arranged the epiphyses in the order in which they ossify in the normal child, according to the data of Hodges.[12] The cases of congenital hypothyroidism are arranged according to the age at which treatment of the patient was begun and the cases of juvenile hypothyroidism according to the age that the deficiency became manifest in the patient as judged by the clinical history.

The symbols under each column indicate whether the particular epiphysis developed in a normal or an abnormal manner, as shown by the study of serial roentgenograms. The symbols +, + + and + + + indicate the occurrence of varying degrees of epiphysial dysgenesis, while N shows that when ossification in the epiphysis was first seen in the roentgenogram the structure was apparently normal. O indicates that ossification was not found in the most recent roentgenogram taken. Those epiphyses which were already ossified before thyroid treatment was begun are indicated by primes. Thus, N′ shows that a normal epiphysis was already present before treatment and +′ that an epiphysis showing dysgenesis was present, while N and + indicate the con-

12. Hodges, P. C.: An Epiphysial Chart, Am. J. Roentgenol. **30**:809, 1933.

TABLE 2.—*Distribution of Epiphyses Showing Dysgenesis in Twenty-Five Hypothyroid Children*

Case	Onset of Hypothyroidism	Age When Treatment Began	Osseous Age When Treatment Began	Present Age Yr.	Present Age Mo.	In Utero: Cuboid Bone	In Utero: Distal Epiphysis of Femur	In Utero: Proximal Epiphysis of Tibia	1-3 Mo.: Head of Humerus	2-10 Mo.: Capitate and Hamate Bones	5-7 Mo.: Head of Femur	6-24 Mo.: Distal Epiphysis of Radius	11-24 Mo.: Capitellum of Humerus	13-24 Mo.: Tuberosity of Humerus	18-24 Mo.: Distal Epiphysis of Tibia	18-24 Mo.: Distal Epiphysis of Fibula	2-3 Yr.: Metacarpal Bones Phalanges of Hand	2-3 Yr.: Triquetrum	3-4 Yr.: First and Second Cuneiform Bones of Foot	3-4 Yr.: Navicular Bone	3-4 Yr.: Greater Trochanter	3-4 Yr.: Proximal Epiphysis of Fibula	4-5 Yr.: Patella	5-6 Yr.: Multangular Bones	5-6 Yr.: Distal Epiphysis of Ulna	7-8 Yr.: Epiphysis of Os Calcis	9-10 Yr.: Trochlea of Humerus	9-10 Yr.: Olecranon	10 Yr.: Pisiform Bone
1	B	7 mo.	<B		9	++′	N?′	++	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O
2	B	11 mo.	<B	7	4	N	++′	O	N	O	N	N	O	N	+++	N	N	N	N	N	N	N	N	N	N	O	N	O
3	B	12 mo.	<B	2		++	+	±	N	±	±	N	O	N	N	O	O	O	O	O	O	O	O	O	O	O	O	O
4	B	14 mo.	<B	3	3	N′	±′	±	N	++	N	N	N	N	N	N	N	N	O	O	O	N	O	O	O	O	O	O
5	B	15 mo.	B	6	9	N′	N′	N?	++	N?	N	N	N	N	O	O	O	O	O	O	O	O	O	O	O	O	O	O
6	B	19 mo.	<B	8	4	N′	++′	+	+	+++	N	N	+	N	N	N	N	++	+	N	++	N	N	N	O	O	O	O
7	B	20 mo.	<B	6	9	N′	N′	O	O	O	O	O	O	O	O	O	N	N	N	N	N	N	N	N	O	O	O	O
8	B	24 mo.	6 mo.	7		N′	N′	O	N′	O	O	O	O	O	O	O	N	N	N	N	N	N	N	N	O	O	O	O
9	B	25 mo.	B	6	6	N′	N′	O	++	O	+	N	+	+	N	N	N	N	N	N	N	N	O	O	O	O	O	O
10	B	28 mo.	9 mo.	5	5	N′	N′	±	N′	+++	N	N	++	+++	±	N	+	O	O	O	O	O	O	O	O	O	O	O
11	B	28 mo.	12 mo.	3	5	N′	N′	++′	N′	+++′	+	++′	++	++′	+	+	N	N	N	O	N	O	O	O	O	O	O	O
12	B	4 yr. 9 mo.	3 mo.	5	6	N′	N′	+++′	+	+++	+	N	N?	N	O	+	+	O	O	O	O	+	O	O	O	O	O	O
13	B	5 yr. 10 mo.	5 mo.	7	9	N′	N?′	+++′	N	+++	+++	+++	+++	+++	+++	N	+++	+++	+	N	+	N	O	O	O	O	O	O
14	<1 yr.	6 yr. 1 mo.	9 mo.	7		N′	±′	++′	N	+++′	±	N	++	±	+++	++	+	N	±	O	O	O	O	O	O	O	O	O
15	<1 yr.	8 yr. 11 mo.	2 yr.	10	8	N′	±′	+++′	±′	+++′	±′	±′	++′	+′	+++	+	±	++	±	++	+	+	±	++	O	O	O	O
16	B?	24 yr.	12 yr.	24		N′	N′	N′	N′	++′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′
17	3 yr.	12 yr.	5½ yr.	14		N′	N′	N′	N′	O	N′	N′	N′	N′	N′	N′	N′	+++′	O	++′	++′	++	+	++	±	+	++
18	4½	8 yr. 9 mo.	4	12	4	N′	N′±	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	±′	N′	++′	N	N	++	±	N	N
19	6 ?	13 yr. 5 mo.	6½	14	5	N′	+′	++′	N′	+′	N?′	++′	++′	N′	N′	N′	N′	N′	++′	N′	+++′	N′	+′	++′	+++′	++′	N
20	6	10 yr. 6 mo.	7	10	6	N′	N′	N′	N′	N?′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	O	++′	O	O	O
21	7	13 yr.	10	13		N′	N′	N′	N′	+++′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	±′	±′	±′
22	10	14 yr. 8 mo.	10	15	6	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N?′	±′	+′
23	B	4 yr.		14		N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	+++′	+′	±′	++′	+++	N	±	+	O	O	O
24	3	7 yr.		13		N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	N′	+++′	±′	N′	++′	N′	N′	N′	N′	O	N′	O
25	?	?		13		N′	±′	±′	N′	±′	N′	±′	±′	N′	N′	N′	N′	N′	++′	±′	++′	+++′	±	±	++	O	O	O	O

B indicates at birth; O denotes that ossification has not occurred; N′ indicates a center of ossification showing normal structure before treatment; N, a center of ossification developing normally during treatment; +′, a center of ossification showing dysgenesis before treatment, and +, a center of ossification developing dysgenetically during treatment. A line encloses those centers which normally should have been ossified at the age when treatment was begun.

dition of epiphysis ossified under treatment. When roentgenograms of particular epiphyses were not taken or when such long intervals elapsed between roentgenograms that the early appearance of the center was not observed, blanks are left on the table, as in cases 7 and 8.

FREQUENCY AND CHARACTER OF THE LESION IN THE VARIOUS EPIPHYSES

The frequency with which dysgenesis was found and the character of the roentgenographic changes observed varied with different osseous centers. The cuboid and the femoral and tibial epiphyses of the knee are usually ossified at birth, although occasionally ossification is absent in normal newborn infants. Dysgenesis of these centers was found only in the younger cretins studied. Multiple foci of ossification in the cuboid bone were found before treatment in 1 cretin of 7 months (case 1, *A*, fig. 3). In another cretin of 12 months (case 3) ossification of the cuboid was absent before treatment but appeared from multiple centers shortly after. Dysgenesis of the centers of the knee was found in 4 young cretins (cases 2, 3, 4 and 6). The abnormality was not marked, consisting of porosity and fluffiness rather than islet formation. The involvement of these centers, which are usually ossified prenatally, may point to the intrauterine existence of hypothyroidism but cannot be accepted as proof, because occasionally ossification of one or more of these centers is absent in normal children at birth. In 2 older cretins (cases 14 and 15) and in 2 children with acquired hypothyroidism (cases 18 and 19), thyroid therapy caused the centers of the knee to grow rapidly, and the newly formed bone at the periphery appeared spongy and irregular (*A*, fig. 4).

Dysgenesis was found more frequently in the head of the humerus and head of the femur than in any other location. These epiphyses were abnormal in 10 out of 12 cretins of whom roentgenograms were made at the proper time for detection of malformation. The abnormality is probably more easily observed in these locations than elsewhere, because these structures are large and continue to grow for a long period. The structural lesions were more spectacular and severe in the femur than in the humerus. (Compare fig. 1 and fig. 5.) In the untreated patients the abnormality persisted for a long time in both locations, being present in the older cretins between 5 and 9 years of age. Under treatment it disappeared rapidly in the head of the humerus but slowly in the head of the femur. Dysgenesis of the capital epiphysis of the femur was usually accompanied by changes in the neck of the femur with coxa vara. The possibility that the severity and the long duration of the lesion in the hip may be related to the mechanical stresses of weight bearing will be discussed later. In a 24 year old untreated cretin (case 16) there

were marked changes in both hips, although the epiphyses elsewhere were of normal structure.

The navicular bone of the tarsus showed marked structural changes and alterations in shape, with appearances of fragmentation resembling

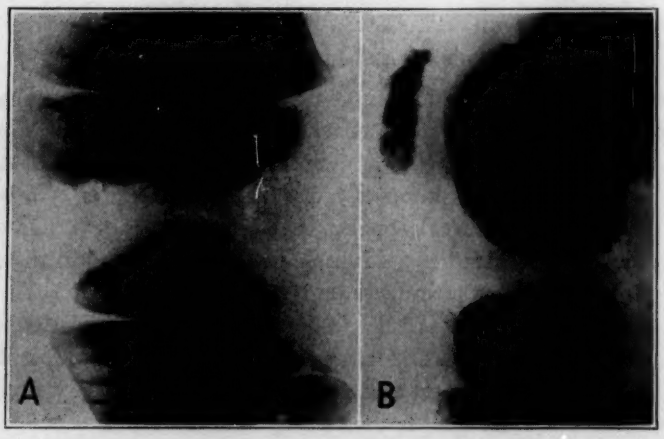

Fig. 4.—Dysgenesis of centers of ossification of knee. *A* (case 15), in hypothyroid dwarf aged 9 years 2 months, three months after treatment was begun; the proximal epiphysis of fibula shows multiple foci of ossification; epiphysis of femur has grown rapidly and margins have become porous and irregular. *B* (case 19), in untreated hypothyroid dwarf aged 13 years 6 months; patella shows irregularity and stippling.

Fig. 5.—Dysgenesis of head of humerus. *A* (case 11), in cretin; aged 2½ years, one month after treatment was begun; head of humerus showed small, discrete centers of ossification before treatment which are now coalescing, giving a fragmental appearance. *B* (case 19), in untreated hypothyroid dwarf aged 13½ years; note spongy appearance of head of humerus.

that in Köhler's disease. However, the abnormality was always bilateral. In the untreated or inadequately treated patients the lesions of the

navicular bone were of longer duration than those of the other tarsal bones. In case 17 the abnormal appearance of the navicular bone was observed to remain unchanged for at least fourteen months, during eight months of which the patient received injections of an extract of the anterior lobe of the pituitary. Three months after thyroid treatment was begun the normal structure of the bone was restored. Mechanical forces perhaps contribute to the duration and severity of the involvement of the navicular bone, as in the case of the hip.

The medium-sized epiphyses of the long bones, such as the distal epiphyses of the radius, ulna, tibia and fibula, the capitellum and the proximal epiphysis of the fibula, and the smaller structures, such as the carpal bones, the cuneiform bones of the feet and the epiphyses of the metacarpal bones and phalanges, showed less frequent and less severe lesions than the larger bony structures previously discussed. In the small round bones the beginning of ossification in multiple foci was noted, but other alterations in the architecture were not observed. Under treatment the entire process, from the earliest appearance of multiple foci of ossification to the completion of the normally formed bone, took place rapidly. It is probable that in certain patients the abnormality was not discovered because roentgenograms were not repeated with sufficient frequency.

The development of the medium-sized epiphyses of the long bones took place more slowly, so that different steps in the process were observed. In the early stages multiple foci of ossification were seen; later, when these had coalesced into a single center, abnormalities in structure still persisted.

The significance of deviations from the normal structure in the parts which ossify later, such as the greater tuberosity of the humerus, the greater trochanter of the femur, the epiphysis of the os calcis, the trochlea, the olecranon and the patella (which is a sesamoid bone), is sometimes difficult to interpret, because these structures normally show irregularities in their methods of ossification. In the normal child, ossification of the trochlea and the olecranon often proceeds from two or three separate centers, and the epiphyses of the os calcis and the patella are more or less irregular in outline. The diagnosis of dysgenesis of these epiphyses was made in the cases reported only when stippling and porosity were marked, as shown in *B*, figure 4.

RELATION OF THE EPIPHYSES AFFECTED TO THE SPAN OF LIFE DURING WHICH HYPOTHYROIDISM EXISTED

The patients whose data are recorded in table 2 may be divided into those who had thyroid deficiency from birth or shortly thereafter and those who probably became deficient later in childhood.

Patients 1 to 16 were probably hypothyroid from birth. All showed marked delay in the appearance of centers of ossification before treatment. The younger ones (patients 1 to 10), in whom few of the epiphyses had ossified after birth, had few evidences of dysgenesis in the roentgenograms taken before treatment. The older ones (patients 11, 12, 13, 14 and 15) showed dysgenesis in most of the cartilages which had ossified before thyroid medication was begun. (Patient 16, who was 24 years old, is an exception.) Many of the new centers of ossification which appeared when treatment was begun showed dysgenesis. The number and distribution of the epiphyses affected depended on the age of the patient when treatment was started, the older patients showing more widespread involvement than the younger ones. A study of table 2 shows that as a rule only those centers in which ossification had been delayed as a result of hypothyroidism showed abnormalities when they ossified subsequently under the influence of thyroid therapy. Centers of ossification appearing later, in cartilages in which ossification normally would not have been expected at the age when treatment was begun, showed no abnormality. For example, patient 3, who was first treated at 12 months of age, showed abnormalities only of those centers of ossification which normally develop during the first year of life, while patient 15, who was not treated until he was about 9 years old, showed dysgenesis of all the epiphyses which ossify during the first eight years.

Patients 2, 6 and 16 are exceptions to the general rule and must be considered separately. The reason for the exception in the case of patient 6 is easy to understand. This cretin was first treated at 14 months of age, and the epiphyses which ordinarily ossify before the twenty-fourth month showed dysgenesis when ossification appeared under treatment. The epiphyses which ossify during the third year then ossified normally. Thyroid treatment was discontinued at the age of 4 years. Growth and development then stopped and symptoms of hypothyroidism reappeared. When medication was resumed at 4 years 8 months of age, the navicular, greater trochanter and patella, which should have ossified during the time treatment lapsed, ossified in the characteristic dysgenetic manner, while ossification of the epiphyses developing later proceeded normally. Patient 2 was a cretin who received unusually intensive treatment, beginning at 11 months of age. Many centers ossified prematurely, so that her osseous development was that of a 5 year old child when she was 17 months old. Several of the epiphyses of the metacarpal bones and phalanges, which ossified prematurely, showed multiple foci of ossification, although ossification in others proceeded normally. I have no explanation to offer. Patient 16 stands out in marked contrast to the rest of the group. She was 24 years old, had never been treated and had the characteristics of a cretin. Her

height was that of an average 8 year old girl, and her mental age was 6½ years. Although an accurate history of her earliest development could not be obtained, it seems probable that her thyroid deficiency dated from birth. Roentgenograms showed that the osseous development was that of a 12 year old child and that no epiphysial fusion had occurred. All of the epiphyses ossifying in childhood were of normal structure except the heads of both femurs, which showed marked irregularities resembling fragmentation. Since hypothyroidism had apparently existed from early infancy, it seems probable that many other epiphyses had ossified in an abnormal manner but, in the course of years, had eventually become normal in appearance. The abnormality of both femoral epiphyses might have been caused either by persistence of the dysgenetic lesion or by a degenerative change which had occurred later in life.

Patients 17 to 22 constitute a group in which hypothyroidism was apparently of the acquired rather than of the congenital type. In all of them except patient 19 the onset could be dated fairly accurately, at an age varying from 3 to 10 years, by cessation in growth and development and by a change in the patient's temperament, activity and appearance. In these patients the occurrence of dysgenesis only in those epiphyses which ossify in later childhood was in marked contrast to its presence in the earlier ossifying epiphyses of the patients with congenital hypothyroidism. Patient 19 possibly should not be included among the patients with juvenile hypothyroidism as the time of onset of the deficiency cannot be accurately established. It was stated that she had learned to sit alone at 6 months, to walk at 14 months and to talk at 14 months. Her parents, who were often inaccurate in their statements, considered that she was always "a small child," but until she was 6 years old they did not notice that she had practically ceased growing. When first examined, at the age of 13 years 5 months, she had marked signs of hypothyroidism. Her height was that of a 6½ year old girl. Her deciduous teeth were all present and carious. Her osseous age was 7 years. The fact that widespread epiphysial dysgenesis was found in the structures which ossify early as well as in those which ossify late suggests that hypothyroidism had existed from a much earlier age than the parents' observations indicate.

Patient 21 deserves special consideration because of the finding of a unilateral lesion, in the head of the right femur. This child grew and developed normally until she was 7 years old. At that time, in June 1933, limp and pain in the right hip developed, and ulcers appeared on both corneas. Roentgenograms taken seven weeks later at a hospital in Washington, D. C., showed no changes in the hips. At about the same time as the onset of these symptoms, marked constipation and dryness of the skin were noted, and she stopped growing. In March

1934 another roentgenogram showed flattening and fragmentation of the head of the right femur, which was believed due to Perthes' disease. In March 1935 she entered another hospital, where the presence of hypothyroidism was suspected. She was given 1 to 2 grains (0.06 to 0.13 Gm.) of thyroid daily, and in the next six months grew 1½ inches (3.6 cm.). The condition of her eyes improved, and the bowel action became regular. After leaving the hospital, administration of thyroid was discontinued and has not been resumed since. When she came under my observation, in January 1940, at the age of 13 years, she had classic signs of hypothyroidism. The concentration of serum cholesterol was 460 mg. per hundred cubic centimeters, and her basal metabolic rate was — 38 per cent. Her height was that of a 7¾ year old girl. Her osseous age was 10 years. The trochlea, olecranon and pisiform bone, which ossify at 9 or 10 years, showed evidences of dysgenesis. All other

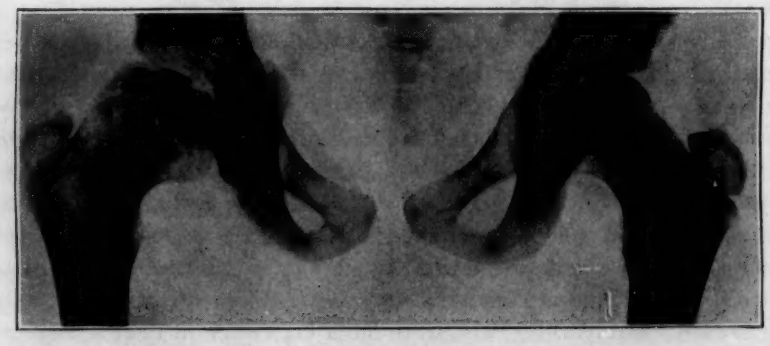

Fig. 6 (case 21).—Osteochondritis deformans of right hip in a hypothyroid girl aged 13. Pain developed in the right hip at 8 years of age, and a roentgenogram taken then showed that both femoral epiphyses were normal. The change in the hip is a degenerative lesion and not dysgenesis.

osseous structures were normal, except the right hip. The roentgenographic appearance of the hips was identical with that in a roentgenogram taken in Washington, D. C., in 1934. The left hip was apparently normal, the head of the femur showing no structural changes. The head of the right femur (fig. 6) was broad and flattened, irregular in structure and of fragmented appearance. The neck of the femur was broad and misshapen. The acetabulum appeared eroded, and the ischium showed areas of rarefaction. This patient was the only one in my series who had a unilateral lesion. Although the roentgenographic appearance of the lesion does not distinguish it from that of certain stages of epiphysial dysgenesis, the fact that the hip was normal in a previous roentgenogram proves that the lesions were due to a destructive process rather than to an abnormality of ossification. Even without such complete evidence,

one would suspect that the lesion was destructive because the patient did not show hypothyroidism until she was about 8 years old, an age when the head of the femur is already well developed, and because the head of the left femur and the other structures which ossify early were normally formed. This observation indicates that true osteochondritis deformans (Perthes' disease) may occur occasionally in the course of hypothyroidism, although it is certainly less common than epiphysial dysgenesis.

Patients 23, 24 and 25 were the only persons included in this study who were receiving thyroid treatment at the time they first came under my observation. The fact that they still had definite signs of hypothyroidism suggests that treatment had been inadequate. Because of the previous treatment of these patients, one can draw no conclusions concerning the relation of the epiphyses involved and the span of life during which hypothyroidism had existed.

EPIPHYSIAL DYSGENESIS IN CONDITIONS OTHER THAN HYPOTHYROIDISM

There are a number of lesions of the epiphyses the roentgenographic appearance of which may resemble that of certain stages of the dysgenesis which I have described. The most common of these is osteochondritis deformans, to which the names of Perthe, Köhler, and Osgood and Schlatter have been applied, the name depending on the bone involved. However, osteochondritis deformans is a destructive lesion which occurs in a previously normal epiphysis. It is usually, but not always, unilateral and generally occurs in only one epiphysis, such as the head of the femur or the navicular bone of the foot. It is generally accompanied by pain. Although this condition may occasionally occur coincidentally with hypothyroidism in children (case 21), or may perhaps be caused by hypothyroidism, it should be differentiated from the abnormality of endochondral ossification described as epiphysial dysgenesis. I have occasionally seen in children with no evidences of hypothyroidism an abnormality in the architecture of the epiphysial centers of ossification and the round bones which produces a spongy or porous appearance, somewhat resembling epiphysial dysgenesis. The cause of such structural changes is unknown. I wish to stress, however, that true epiphysial dysgenesis can be differentiated with certainty from other conditions which might simulate it in a single roentgenogram only by following the stages of ossification in serial roentgenograms. It must also be remembered that certain structures, such as the olecranon, the trochlea, the patella and the epiphysis of the os calcis, occasionally ossify normally from two or three well defined foci instead of from a single center. Sometimes ossification in the head of the humerus or in some

other structure may appear as a number of minute, closely crowded points of calcification, which rapidly unite into a single center. There is no reason to mistake these isolated instances of multiple foci of ossification for true epiphysial dysgenesis, which affects many different bones

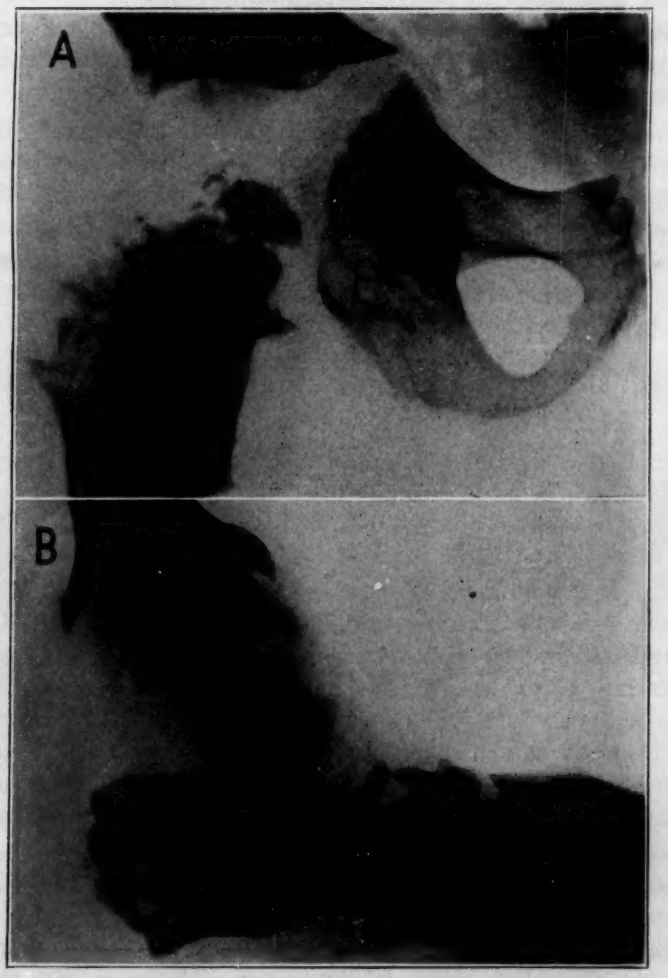

Fig. 7.—Chondrodystrophy, showing multiple foci of ossification. *A*, in head of femur. *B*, in epiphysis of fibula.

and is characterized by the appearance of numerous small, irregular islets of ossification scattered over a fairly large area. It is true that widely separated irregular islets of ossification occur in the epiphyses in cases of chondrodystrophy (fig. 7). However, the grotesque deformities of the metaphyses and shafts of the long bones and the grossly abnormal shapes of the epiphyses make it easy to recognize this condition.

Although I have examined hundreds of roentgenograms of normal children, of dwarfs and of children with bone dyscrasias, I have failed to find the characteristic lesions of true dysgenesis in any condition except hypothyroidism. Ecke [13] studied 11 midgets roentgenologically. They all showed marked retardation of osseous development and, in addition, abnormalities in the epiphyses of many bones, especially the hips and the navicular bone of the foot. One cannot be sure from the roentgenographic appearance whether these structures had ossified in the manner characteristic of epiphysial dysgenesis or whether they had ossified in a normal manner and had subsequently undergone destructive change. The high incidence of the condition in these subjects suggests that it was brought about by whatever caused the dwarfism. Although clinically these midgets had no obvious signs of hypothyroidism, biochemical and metabolic studies were not made, and one cannot exclude the possibility that secondary hypothyroidism existed.

In dwarfs who had no clinical or biochemical evidence of hypothyroidism I have frequently encountered evidence of delay in the ossification of cartilages to as marked degree as in the hypothyroid dwarfs. However, in such patients epiphysial dysgenesis was not found either before treatment or with thyroid therapy.

COMMENT

My studies confirm the conclusions of other writers that epiphysial dysgenesis is apparently due to an abnormality of endochondral ossification, which causes deposition of calcium to begin in multiple irregular foci covering a large area instead of in a single, small nucleus. The roentgenologic appearance depends on the stage of calcification when the roentgenogram is made. In the 25 cases reported the abnormality was found in all hypothyroid children in whom roentgenologic studies were made frequently enough to record the early stages of epiphysial ossification. The disturbance probably affects all endochondral ossification throughout the skeleton. When a roentgenogram is taken before treatment, cartilaginous centers which have ossified during the untreated phases of the disease are found to be abnormal. When adequate treatment with thyroid is begun and new centers of ossification appear, those parts which ossify first show dysgenesis, while those which ossify later develop normally. The epiphyses showing dysgenesis are those which ordinarily should have calcified during the years when hypothyroidism remained untreated. The normal structures are those in which ossification would not have occurred until after the thyroid deficiency was corrected.

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13. Ecke, W.: Zur Morphologie und Genese des Zwergwuchses: Untersuchungen an Liliputänern, Fortschr. a. d. Geb. d. Röntgenstrahlen **60**:107, 1939.

These facts suggest that during the untreated phase of hypothyroidism those cartilages in which calcification has been delayed undergo some change which is not recorded in the roentgenogram. In normal bone formation cartilage passes through a cycle of histologic alterations preliminary to calcification and ossification. That these preparatory stages are disturbed by hypothyroidism is suggested also by the fact that calcification finally occurs in multiple foci scattered over a large area instead of in a single, small nucleus which grows in an orderly fashion. This theory is illustrated schematically in figure 8, but my studies do not permit me to deduce the histologic nature of the changes in the cartilage.

The histologic studies of cartilage in cases of hypothyroidism which have been reported do not throw much light on epiphysial dysgenesis.

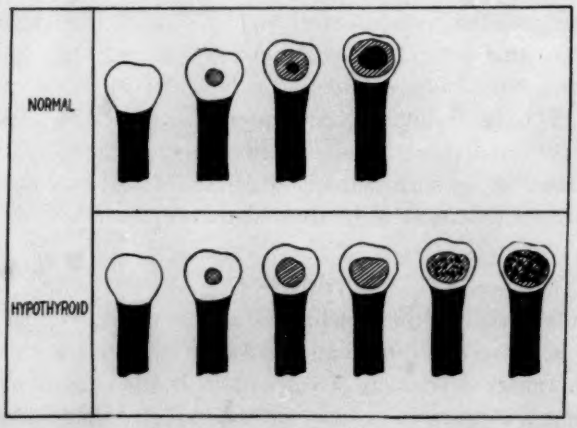

Fig. 8.—Diagrammatic representation of ossification of epiphysis in normal and in hypothyroid subjects. Shaded areas represent change which occurs in epiphysial cartilage preparatory to ossification; black areas represent calcification. In normal bone calcification occurs from a single nucleus in the cartilage which has undergone the preparatory change. In hypothyroidism, there is an abnormality in the preparatory stage and calcification is delayed, occurring finally from multiple foci scattered over a large area.

Langhans,[14] in 1897, and Dieterle [15] and Wegelin,[16] in 1906, described only the changes in the epiphysiodiaphysial junction of the long bones.

14. Langhans, T.: Anatomische Beiträge zur Kenntnis der Cretinen, Virchows Arch. f. path. Anat. **149**:155, 1897.

15. Dieterle, T.: Die Athyreosis unter besonderer Berücksichtigung der dabei auftretenden Skelettveränderungen, sowie der differential-diagnostisch vornehmlich im Betracht kommenden Störungen des Knochenwachstums, Virchows Arch. f. path. Anat. **184**:56, 1906.

16. Wegelin, C.: Schilddrüse, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1926, vol. 8, p. 470.

Lang,[17] in 1922 examined the hip of a 10 year old cretin whose femoral epiphyses showed no ossification. The cartilage contained irregular areas of poorly stained tissue alternating with areas taking an intense basophilic stain. In places the cartilage had apparently disintegrated and had been replaced by cystic areas filled with dark-staining fluid. The deeply basophilic portions of the cartilage, being well vascularized and containing hypertrophied cartilage cells, seemed to be the seat of proliferative changes preparatory to ossification. Looser,[4] in 1929, also made histologic studies of the femoral epiphysis of cretins and found that ossification did not proceed from a centrally located and concentrically enlarging zone of calcification. He observed that irregular ossification occurred, resulting in the persistence of islets of cartilage, often large and roentgenographically discernible. Liquefaction and fibrotic changes in the cartilage seemed to be responsible for the formation of fissures and, at times, actual fragmentation of the epiphyses with the liberation of joint bodies. He expressed the belief that weight bearing and stresses caused the diseased epiphyses to become crushed and flattened. More detailed studies than those already reported will be required to show the exact nature of the disturbance which probably occurs in the cartilage preparatory to calcification and ossification.

Although the primary factor in epiphysial dysgenesis is a disturbance occurring in the cartilage before ossification, the additional influence of mechanical forces and strains on certain of the abnormally formed epiphyses must be taken into consideration. The head of the femur and the navicular bone of the foot are the most important weight-bearing bones of the body. These parts show structural lesions which are more severe and persist longer than any others, irrespective of treatment. In a 24 year old untreated cretin (patient 16) marked structural abnormalities were found only in the heads of both femurs, although presumably other centers had ossified abnormally and undergone restitution. In patient 21 there was conclusive evidence that the changes in the right hip were due to a destructive process occurring in an epiphysis which had ossified normally. Whether the abnormality was entirely coincidental or whether thyroid deficiency caused some weakening in the normally formed but still growing epiphysis is debatable. Benjamin and Miller[10] reported on a cretin of 11 years whose treatment with thyroid had been started at 17 months but had been irregular after the eighth year. After an injury a slipping of a femoral epiphysis had occurred. They concluded that hypothyroidism had caused the formation of a weakened diaphysioepiphysial cartilage. Although such lesions are quite distinct from true epiphysial dysgenesis,

17. Lang, F. J.: Mikroskopische Befunde bei juveniler Arthritis deformans (Osteochondritis deformans juvenilis coxae Legg-Calve-Perthes), nebst vergleichenden Untersuchungen über die Femurkopfepiphyse mit besonderer Berücksichtigung der Fovea, Virchows Arch. f. path. Anat. **239**:76, 1922.

the fact that true destructive unilateral osteochondritis deformans of the Perthes type or a slipped femoral epiphysis may occur occasionally in hypothyroidism is worthy of note.

SUMMARY

Epiphysial dysgenesis associated with hypothyroidism is manifested in roentgenograms by the appearance of multiple irregular islets of ossification in the cartilages scattered over a large area. These enlarge and coalesce to form an irregular, spongy, porous or fluffy mass. All centers of endochondral ossification may be affected. The abnormality was found in 23 of 25 hypothyroid children of whom roentgenograms were made at frequent intervals after treatment was begun. It was found not only in cartilages which already were ossified prior to thyroid treatment but also in those which began to ossify during the course of therapy. Only those centers showed dysgenesis in which the appearance of ossification had been delayed as a result of hypothyroidism. With continued treatment, ossification took place normally in those centers which ordinarily would not have been ossified at the age when therapy was begun. These observations suggest that in hypothyroidism a disturbance occurs in the cartilage in a stage just prior to the beginning of calcification.

In 1 hypothyroid child true osteochondritis deformans of one hip was found. This is a destructive lesion in a normally formed epiphysis and should be differentiated from epiphysial dysgenesis, which is an abnormality in endochondral ossification. Osteochondritis deformans and certain structural irregularities of the epiphyses may simulate epiphysial dysgenesis in a single roentgenogram. I have never found unquestionable epiphysial dysgenesis in any condition except hypothyroidism. It was not found in dwarfs who did not have hypothyroidism even when they had delayed osseous development.

DISCUSSION

DR. ARTHUR H. PARMALEE, Oak Park, Ill.: I should like to ask Dr. Wilkins whether it was noted that there were changes at the point of junction of the shaft with the epiphysis. Some have described the so-called annual lines as being due to hypothyroidism, and it is reasonable to expect that if this change occurs in the bone formation or calcification of the cartilage at the epiphysial center it might occur also at the junction of the shaft with the epiphysis.

DR. LAWSON WILKINS, Baltimore: You mean the transverse line?

DR. ARTHUR H. PARMALEE, Oak Park, Ill.: Yes.

DR. LAWSON WILKINS, Baltimore: Specific changes were not noted at the epiphysial line. The transverse lines of retarded growth described in detail by Drs. Park and Eliot are found very commonly in hypothyroidism but are not specific.

It is quite possible that some weakening or destruction of the cartilage at the epiphysial line may occur which does not show in the roentgen picture. This may account for the slipped femoral epiphyses sometimes encountered in patients with hypothyroidism. A case was described by Benjamin and Miller, in Brooklyn.

A TOXIC FACTOR IN THE STOOLS OF PATIENTS ILL WITH POLIOMYELITIS

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AND
WILLIAM S. TAKACS, B.S.
CLEVELAND

It has been suggested that there is a toxic factor in the stools and urine of patients with poliomyelitis,[1] the effects of which can be neutralized by the previous injection of convalescent poliomyelitis serum, although not by serums obtained during the acute stage of the disease.[2] Kramer and associates [3] have alluded to this toxic factor. It causes depression of the rabbit's intestine—a depression which is prevented by convalescent poliomyelitis serum.[4] No specimen obtained from human beings ill with other contagious diseases, except influenza, contains a like factor. It has been found in the stools of monkeys ill with experimental poliomyelitis and not in those of normal animals.

The colon bacillus is present in these fecal specimens, and in this connection it has been shown that as patients with poliomyelitis become better there is a rise in the agglutinin titer of their blood serums against enteric organisms.[5] Normal horse serum has a high agglutinin titer against the enteric group of organisms and has been used successfully to neutralize the toxic factor found in stools from patients ill with poliomyelitis.[6]

Aided by a grant from the National Foundation for Infantile Paralysis, Inc.

From the Division of Contagious Diseases, City Hospital, and the Department of Pediatrics, Western Reserve University School of Medicine.

1. Toomey, J. A.: Demonstration of a Toxic Factor in the Stools and Urines of Poliomyelitis Patients, J. Prev. Med. **6**:379, 1932.

2. Toomey, J. A.: Neutralization Experiments in Poliomyelitis: Results of Injections of Stool Emulsions in Animals Previously Passively Immunized with Convalescent Poliomyelitis Serum, J. Prev. Med. **6**:397, 1932.

3. Kramer, S. D.; Hoskwith, B., and Grossman, L. H.: Detection of the Virus of Poliomyelitis in the Nose and Throat and Gastrointestinal Tract of Human Beings and Monkeys, J. Exper. Med. **69**:49, 1939.

4. Toomey, J. A., and von Oettingen, W. F.: An Enterodepressant Factor in the Stools and Spinal Cords of Monkeys Infected with Poliomyelitis, Am. J. Dis. Child. **48**:30 (July) 1934.

5. Toomey, J. A.: Changes in Titers of Agglutinins for Enteric Organisms in the Blood Serum in Poliomyelitis, J. Infect. Dis. **54**:74, 1934.

6. Toomey, J. A.: Neutralizing Value of Various Substances Against Lethal Doses of: (A) Stool Emulsions from Patients with Poliomyelitis and (B) Colon Paratyphoid Organisms, Am. J. Dis. Child. **48**:1284 (Dec.) 1934.

When standardized emulsions of stools from patients with poliomyelitis were injected into guinea pigs there was an increase in the number of deeply staining lymphocytes in the gray and white matter of the cord. Absence or relative decrease of all motor cells was noted or, if no decrease in number, varying stages of cell destruction. At times the motor cells had homogeneous, blurred cytoplasm, with hazy outlines, and indefinite nuclei which usually were not pyknotic but rather approached the stage of karyolysis. There was a marked increase in the capillaries of the gray matter in 75 per cent of the specimens.[7]

It was but a step further to show that the products of gastrointestinal organisms accelerate the production of poliomyelitis.[8]

It was decided to reinvestigate this toxic factor to determine its presence or absence and whether its addition to poliomyelitis virus might activate the latter sufficiently to produce the disease in guinea pigs.

TABLE 1.—*Results of Injection of Emulsions of Stools from Patients Ill with Poliomyelitis and from Guinea Pigs Dying from Those Injections*

Generation	No. of Animals Receiving Injections	Results		
		Died Within 4 Days	Lived	Died After 4 Days
1	10	10 (100%)	0	0
2	15	14 (93.3%)	1	0
3	15	13 (86.6%)	2	0
4	9	8 (88.8%)	1	0
5	5	5 (100%)	0	0
6	5	4 (80%)	0	1
7	5	0	3	2
8	5	0	5	0

EXPERIMENTAL PROCEDURES

EXPERIMENT 1.—The first objective was to determine again if there was any toxic factor present in the stools of guinea pigs after they had received injections of poliomyelitis virus. Should this be found, the next step would be to determine in how many generations this factor would persist in the gastrointestinal tract.

Stools from patients with poliomyelitis were pooled and suspended in sterile distilled water; 3 cc. was placed in a Hopkins tube and centrifuged at 2,500 revolutions per minute for one minute, so that the reading would be approximately 0.2 cc. on the tube. Adjustments were then made by adding a physiologic solution of sodium chloride to each specimen until the reading was exactly 0.2 in 3 cc. This amount was injected subcutaneously. The combined contents of the gastrointestinal tracts of the guinea pigs which died in one generation were again standardized as described and injected into another generation of guinea pigs, and so on until the toxicity was lost. The results are outlined in table 1.

7. Toomey, J. A.: Pathologic Reactions in Guinea Pigs Injected with Standardized Stool Emulsions from Poliomyelitis Patients, J. Prev. Med. **6**:387, 1932.

8. Toomey, J. A.: Accelerated Production of Poliomyelitis, Proc. Soc. Exper. Biol. & Med. **31**:1015, 1934.

Toxicity was deemed to be present if the animals died within four days after the injection. From 80 to 100 per cent of each generation among the 57 animals that died succumbed within this time limit. It is noted that the fecal emulsions were toxic for at least six generations.

As controls, 9 normal animals were isolated for two months. They were killed and their stools standardized individually in the same fashion as noted in the foregoing descriptions, and each stool was injected into 5 guinea pigs, making 45 control animals in all.

Two, or 4.4 per cent, died within the first four days. Twenty-four of the animals lived ten days or more. The difference in results with

TABLE 2.—*Results of Injection of Emulsions of Stools of Normal Guinea Pigs*

Stool From Animals	Number of Animals Receiving Injections	Results		
		Died Within 4 Days	Lived	Died After 4 Days
1	5	0	1	4
2	5	0	2	3
3	5	2	1	2
4	5	0	1	4
5	5	0	1	4
6-9	20	0	13	7

TABLE 3.—*Results of Injection of Filtered Emulsions of Stools from Patients Ill with Poliomyelitis and from Guinea Pigs Dying from Those Injections*

Generation	Number of Animals Receiving Injections	Results		
		Died Within 4 Days	Lived	Died After 48 Hours
1	10	4	4	2
2	5	0	3	2
3	5	0	2	3
4	5	0	5	0

control and with experimental animals was obvious, although only relatively great.

EXPERIMENT 2.—This experiment was performed to see if the toxic factor in the stools could be filtered out. Stools were standardized as previously and then filtered, and 5 cc. was injected intraperitoneally. This dose was two-thirds greater than the dose used in the previous experiment. The results are noted in table 3.

The filtrate was toxic in the first, but not after the first, generation. Thus, filtration removes this factor.

EXPERIMENT 3.—Although filtration removed the factor responsible for the normal toxicity of the stools, it was thought the sterile eluate of the stool might be toxic. The stools were standardized as in previous experiments, eluted overnight with disodium phosphite (Na_2HPO_2) and

centrifuged the next morning, and the supernatant fluid was filtered. The filtrate was a sterile, straw-colored fluid. The same procedure was followed as before; the dose was 5 cc. of the sterile eluate. The controls were given injections of an emulsion of the untreated stool.

The results indicate that the sterile eluate was about as toxic as the emulsion of whole stool, which contained intestinal bacteria.

EXPERIMENT 4.—It was thought that the toxic factor might also be present in the brain and spinal cord of guinea pigs, and since the spinal cords and brains of animals were the materials to be used to determine the presence of virus, it was decided to see whether the addition of these

TABLE 4.—*Results of Injections of Emulsion and Eluate of Stools of Patients Ill with Poliomyelitis*

Generation	Material	Number of Animals Receiving Injections	Results		
			Died Within 4 Days	Lived	Died After 48 Hours
1	Emulsion of stool.....	10	5	1	4
2	Filtered eluate of stool.....	10	4	2	4

TABLE 5.—*Results of Injection of Sterile Eluate of Stools of Guinea Pigs to Which a Suspension of Brains and Spinal Cords Had Been Added*

Generation	Number of Animals Receiving Injections	Results		
		Died Within 4 Days	Lived	Died After 48 Hours
1	20	11 (55%)	1	8
2	15	7 (46.6%)	5	3
3	9	6 (66.6%)	3	0
4	5	3 (60%)	1	1
5	5	5 (100%)	0	0
6	5	0	4	1
7	5	0	5	0

ground organs would enhance the toxicity of the fecal eluate. Toxic doses of sterile fecal eluate were injected subcutaneously into guinea pigs and the stools, spinal cords and brains of succeeding generations harvested. The sterile filtered eluate of the stools was obtained and used as a menstruum in which to grind cords and brains. The dose given was 0.2 cc. of ground cord and brain in 3 cc. of sterile fecal eluate. Table 5 gives the results.

The addition of a suspension of cord and brain to the fecal eluate did not enhance its toxicity, for this combination did not kill beyond the seventh generation.

EXPERIMENT 5.—Is the factor in the stool neutralizable by convalescent poliomyelitis serum? Thirty animals were given intraperitoneal injections of 5 cc. of convalescent poliomyelitis serum, 30 were

given 5 cc. of serum taken from normal monkeys and 30 were given 5 cc. of an antipoliomyelitis horse serum.[9] Two days later these 90 animals and 30 normal controls were given subcutaneous injections of 3 cc. of the standard fecal emulsion prepared as previously described. The results are contained in table 6.

The lower mortality in protected animals on or before the fourth day after injection, or even after the fourth day, clearly indicates that some protection was conveyed by specific serums.

TABLE 6.—*Neutralizing Effect of Convalescent Poliomyelitis Serum and Antipoliomyelitis Horse Serum Against the Toxic Factor in Emulsions of Stools of Patients with Poliomyelitis*

No. of Animals	Protecting Material	Results: Died Within 4 Days	Died After 4 Days	Lived	Total Mortality
30	5 cc. antipoliomyelitis horse serum...	5 (16.6%)	7	18	12 (40%)
30	5 cc. convalescent poliomyelitis serum	4 (13.3%)	5	21	9 (30%)
30	5 cc. normal monkey serum.....	7 (23.3%)	8	15	15 (50%)
30	Controls: not protected.....	12 (40%)	9	9	21 (70%)

TABLE 7.—*Neutralizing Effect of Convalescent Poliomyelitis Serum and Antipoliomyelitis Horse Serum Against Toxic Factor in Eluate of Stools of Patients with Poliomyelitis*

No. of Animals	Protecting Material	Results: Died Within 4 Days	Died After 4 Days	Lived	Total Mortality
40	5 cc. convalescent poliomyelitis serum	5 (12.5%)	1	34	6 (15%)
40	5 cc. antipoliomyelitis horse serum...	6 (15%)	5	29	11 (27.5%)
40	Controls: not protected.....	10 (25%)	12	18	22 (55%)

EXPERIMENT 6.—The previous experiment did not settle the question as to whether the neutralized element was the product of bacteria, of virus or of some combination. To rule out the immediate effect of the various enteric bacteria present, an experimental neutralization against sterile fecal eluates was done. Forty animals were each given injections intraperitoneally of 5 cc. of convalescent poliomyelitis serum, and 40 were each given 5 cc. of antipoliomyelitis horse serum. Two days later these 80 animals and 40 unprotected controls were given intraperitoneal injections of 12 cc. of pooled fecal eluate of patients with poliomyelitis. The results are shown in table 7.

9. Toomey, J. A.: Poliomyelitis Antiserum Obtained from Horses, Am. J. Dis. Child. **53**:1492 (June) 1937.

The difference between 15 and 55 per cent is statistically of definite value. The results of these experiments seem to show that the eluate of the stools of patients with poliomyelitis contains a toxic factor which may be eluted as well as neutralized by pooled convalescent poliomyelitis serum.

COMMENT

Stasis of the intestine occurs frequently in patients with poliomyelitis. The toxic factor present in their stools may be due to the enhancement of bacterial virulence of resident organisms. The effect of the bacteria present in the stool did not seem important, since a sterile fecal eluate was just as toxic as the whole stool.

These experiments suggest that convalescent poliomyelitis serum may have the ability to neutralize not only poliomyelitis virus but also a toxic factor present in the gastrointestinal tract. That this is not improbable is seen from the fact that the agglutinin titer against enteric organisms rises as the experimental animal with poliomyelitis gets better.

CONCLUSION

Further evidence is given to support the theory that a toxic factor is present in the stools of patients with poliomyelitis which may be produced as a result of stasis of the intestinal contents or may result from a combination of this stasis and the virus itself. Specific convalescent serum has some neutralizing value against this factor.

EVIDENCE OF MONOZYGOSITY AND DISTURBANCE OF GROWTH IN TWINS WITH PYLORIC STENOSIS

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It has been suggested by Cockayne,[1] Sheldon [2] and Penrose [2a] that the condition of pyloric stenosis has a genetic basis, and although four fifths of the examples occur in males the factor is probably not sex linked. Cockayne added that "the way in which the condition is inherited is still uncertain and an environmental factor may be necessary for its production in addition to the genetic one."

Sheldon collected records of the condition in 36 sets of twins. Although the analysis of the type of twinning is for the most part inadequate, the evidence indicates that in the case of uniovular twins both infants are affected (with 1, or possibly 2, exceptions), while in the case of binovular twins the condition is likely to occur in only 1 infant. Sheldon made the significant observation that in a population of 1,000 infants with pyloric stenosis the proportion of twins to single births is nearly twice the expected number, that is, 1 to 43.4 as compared with 1 to 80.

In the present report, the occurrence of pyloric stenosis in both members of 2 pairs of male twins is described, and the evidence for the diagnosis of their type of twinning is outlined. The frequent inadequacy of the determination of the type of twinning is indicated in the summary of data from 11 cases of pyloric stenosis in possibly monozygotic twins (table 1).

From the Departments of Biology and Paediatrics, University of Toronto, and the Hospital for Sick Children.

1. Cockayne, E. A.: Congenital Pyloric Stenosis in First Cousins, Lancet **2**: 898, 1934; Congenital Pyloric Stenosis in First and Second Cousins, Arch. Dis. Childhood **13**:249, 1938.

2. Sheldon, W.: Hypertrophic Pyloric Stenosis in One of Uniovular Twins, Lancet **2**:1048, 1938.

2a. Penrose, L. S.: Maternal Age, Order of Birth and Developmental Abnormalities, J. Ment. Sc. **85**:1141 (Nov.) 1939.

TABLE 1.—*Data from Eleven Cases of Pyloric Stenosis in Twins Who Were Possibly Monozygotic*

Author	Sex of Twins	Basis of Diagnosis
Moore, H. L.: South. M. J. **17**: 187, 1924	♂ ♂ (Both died)	Type of twinning not stated
Davis, H. H.: J. A. M. A. **83**: 686 (Aug. 30) 1924	♂ ♂ (Both died)	Type of twinning not stated
Lasch, W.: München. med. Wchnschr. **72**: 1155, 1925	♀ ♀ (One normal; the affected one died)	Monochorionic; similar in appearance, shape of skull and iris and hair pigment
Bilderback, J. B.: Northwest Med. **27**: 182, 1928	♂ ♂ (One died)	Type of twinning not stated
Cockayne, E. A., and Sheldon, W.: Proc. Roy. Soc. Med. **21**: 1260, 1928	♂ ♂ (One died)	Monochorionic and diamniotic, by midwife's report
Sommer, R.: Deutsche Ztschr. f. Chir. **232**: 398, 1931	♀ ♀ (Both recovered)	Listed as uniovular but no evidence cited
Varden, A. E.: J. Pediat. **3**: 493, 1933....	♂ ♂ (One died)	Similar in physical examination and in handprints; placenta monochorionic and diamniotic *
Redgate, J. W.: Brit. M. J. **2**: 725 and 973, 1935	♂ ♂ (One died)	One placenta, "with a common circulation," according to statement of obstetrician
de Lange, C.: Arch. Dis. Childhood **11**: 39, 1936	♂ ♂ (Both recovered)	Monochorionic, according to midwife's report
Sheldon [2]	♂ ♂ (One normal; the affected one recovered	Similar in appearance; single placenta, with one set of membranes; fingerprints taken at 4 mo., the "expert report being that the fingerprints and thumbprints of the twins were not facsimiles"
Card, T. A.: J. Pediat. **14**: 658 (May) 1939	♂ ♂ (One died)	Monochorionic, according to statement of obstetrician

* Adequate analysis of twinnings.

TABLE 2.—*Data From Twelve Cases of Pyloric Stenosis in Twins From the Hospital for Sick Children, Toronto*

Year	Initials of Twins	Sex of Twins *	Type of Twinning
1914-1915	R. R.	♂ ♀	Fraternal
1917-1918	R. McG.	♀ ♂	Fraternal
1925-1926	B. M. (twin died; parents described the twins as identical in December 1939)	♂ ♂	Doubtful
	A. G.	♂ ♀	Fraternal
1927-1928	Harvey and Grant I. (reexamined November 1939).....	♂ ♂	Fraternal
1930-1931	Ross and Donald McF. (reexamined November 1939).....	♂ ♂	Fraternal
1933-1934	R. W.	♂ ♀	Fraternal
1935-1936	William and Harry L. (reexamined December 1939).....	♂ ♂	Fraternal
1937-1938	P. W.	♂ ♀	Fraternal
1938-1939	Garry and Glen T. (examined 1938).....	♂ ♂	Identical †
	Robert and Richard G. (examined 1938).....	♂ ♂	Identical †
	Erla and Arla C. (examined 1939).....	♀ ♀	Fraternal

* The symbol — indicates the presence of pyloric stenosis.
† Subjects of this paper.

TWINNING AS AN ETIOLOGIC FACTOR IN PYLORIC STENOSIS

In the past twenty-five years at the Hospital for Sick Children, Toronto, 436 children have been treated for pyloric stenosis. Among these patients were 12 pairs of twins, listed in table 2. Nine of the pairs are known to be fraternal sets, either because of their boy-girl combination or from studies made of their physical features and dermatoglyphic patterns. In the tenth case, in which 1 twin died, the opinion of the parents (given thirteen years later) is that the twins were identical, but under the circumstances the type is recorded as doubtful. The remaining 2 sets (discussed in the present paper) will be shown to be identical.

The proportion of twins in the group of 436 patients is 1 to 36.3, a number more than twice that expected, since in Canada the frequency of twin births is 1 in 83.4. It would seem, therefore, that the environmental handicap imposed before birth on members of multiple sets is one factor inducing the condition of pyloric stenosis.

TWO PAIRS OF MALE TWINS WITH PYLORIC STENOSIS

CASE 1 (Garry and Glen T.).—On Nov. 28, 1938, 8 week old twins (Garry and Glenn T.) were admitted to the Hospital for Sick Children, Toronto. The parents complained that the children had been vomiting in projectile fashion since 19 days of age. The vomiting had begun suddenly on the same day in both children. Two weeks prior to admission a nasal discharge had developed in both children.

The parents were healthy, 23 years old. They had had no serious illnesses, and this was the first pregnancy. The children had been born after an uneventful pregnancy and an easy labor and had weighed 5 pounds 10½ ounces (2,565 Gm.) and 5 pounds 4 ounces (2,381 Gm.), respectively. For the first eighteen days of life they had thrived, had taken their feedings well and had not vomited. After the symptoms of vomiting appeared at 19 days of age their weight remained about stationary, and on admission to the hospital the smaller twin weighed 5 pounds 15 ounces (2,633 Gm.) and the larger 6 pounds 7 ounces (2,892 Gm.).

Physical examination revealed 2 poorly developed and nourished infants showing the sunken-eyed, loose-skinned picture of dehydration. Each had a slight mucoid nasal discharge and mild reddening of the posterior pharyngeal wall. In both children the abdomen was protuberant, and during and after feeding large peristaltic waves could be seen passing from left to right across the upper part of the abdomen. In both a small, firm tumor could be palpated in the right upper quadrant of the abdomen. A provisional diagnosis of pyloric stenosis was made in both cases. The infants were each given fluids intravenously and a small blood transfusion to combat the dehydration.

On December 2 both children were considered in adequate condition for surgical intervention. When the peritoneum was opened a firm tumor the size of an olive was found in both instances. Ramsted's pyloroplasty was performed; the patients were given transfusions and were returned to their beds in good condition.

The children were given ½ ounce (15 cc.) of breast milk every four hours for six feedings, and to this amount was added 1 drachm (3.7 cc.) of breast milk each time that the feeding was kept down. Five days after operation each child was receiving 3 ounces (90 cc.) of breast milk six times a day. The change to a 2 per

cent lactic acid milk feeding was made without upset, and on December 15 both children were discharged to return home, having gained, respectively, 13 and 8 ounces (368 and 226 Gm.) in the thirteen days after operation.

DETERMINATION OF TYPE OF TWINNING OF GARRY AND GLEN T.

Although twins Garry and Glen T. bore a close resemblance in general features, a detailed study of their dermatoglyphic patterns raised some doubts as to their classification. Particularly, they failed to sub-

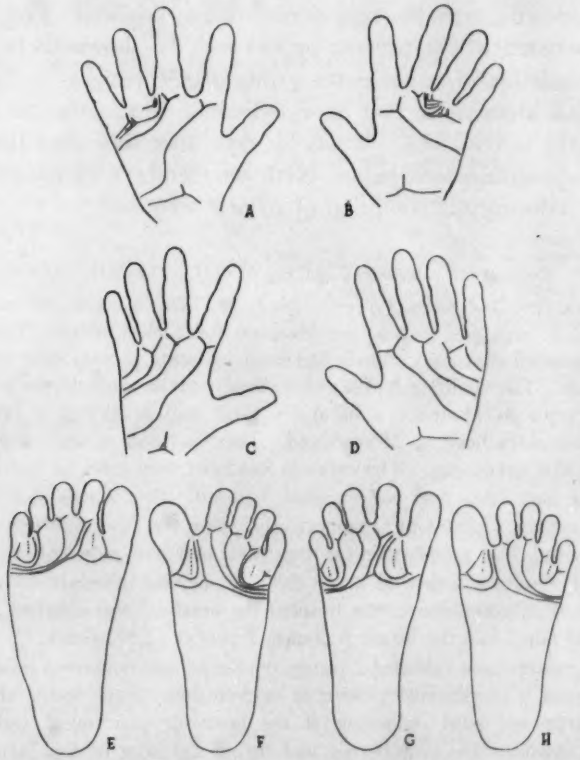

Fig. 1.—Outlines of the palmar and plantar figurations of Garry and Glen T. *A*, *B* are palmar, *E*, *F* are plantar patterns of Garry. *C*, *D* are palmar, *G*, *H* are plantar patterns of Glen.

scribe to the recognized principle that in uniovular twins the configurations of the epidermal ridges of the hands have a close resemblance, which should be greater between the two corresponding hands of the pair of twins than that between the right and left hand of 1 twin. In other words, the bilateral differences should be greater than the homolateral (or, in some cases, the heterolateral). At variance with this principle, Garry and Glen T. showed palmar patterns which were strikingly different (fig. 1 *A* to *D*, table 3), the bilateral differences in their

palmar lines and patterns amounting to 25 and 0 per cent, which is less than the homolateral difference of 57.5 per cent.

It is known that these twins, although monochorionic, had an unusual placenta. The possibility was therefore considered of their being third type twins (Danforth,[3] Fisher,[4] Curtius and Verschuer,[5] Greulich [6]) and thus having an identical maternal but a different paternal inheritance. Such evidence was, however, insufficient.

Placenta.—The placenta of the twins was fortunately available for study, having been injected and preserved at the time of their birth (as part of an investigation into the fetal circulation of multiple sets, a study being made in cooperation with several Toronto hospitals). The fetal membranes presented an unusual arrangement.

The twins were born at the Toronto East General Hospital on Oct. 4, 1938. One amnion had broken five days previously; the second

TABLE 3.—*Palmar Formulas of Twins Garry and Glen T. and of Their Parents and Paternal Grandmother*

		Palmar Main Lines	Axial Triradiuses	Palmar Patterns
Garry T.....	Left	5″-9.9.5″.3	t′	A^u/A^c.O.O.l.O
	Right	11(10).9-7.7(6).5′		
Glen T.....	Left	0.5″.5″.3	t′	A^u/A^c.O.O.l/l.D
	Right	0.5″.5′.3	t	A^u.O.O.O.O
Father.....	Left	9.7/9.5″.4	t	A^u.O.O.O.O
	Right	11.9.7.5′	t′	A^u/A^c.O.d.l.l
Mother.....	Left	11.7.7.1	t′	A^u/A^c.O.D.L.W
	Right	11.7.7.2	tt′	S.O.O.O.L
Paternal grandmother.....			O	A^r.O.O.O.l
	Left	9.7.5″.3	t	A^u/A^c.O.M.O.L
	Right	10.7.5″(6).4	t	A^u.O.M.V.M

broke after the delivery of the first child. The assistant supervisor, Miss J. MacMaster, drew attention to the unusual placenta, which seemed to have "a sac within a sac." The obstetrician, Dr. R. Taylor, also pointed out that "the amnions did not fit back into the chorion." Both these observations proved to be correct. The placenta, which was single and monochorionic, had fitting against the chorion an outer amnion, with a velamentous attachment of the umbilical cord. Enfolded within this amnion was a second amnion, its cord having a central attachment.

A common circulation of the two blood streams was clearly demonstrated when, shortly after delivery, the placenta was injected. A red gelatin mass, forced into one artery of the second cord under a pressure

3. Danforth, C. H.: Is Twinning Hereditary? J. Heredity **7**:194, 1916.

4. Fisher, R. A.: The Genesis of Twins, Genetics **4**:489, 1919.

5. Curtius, F., and Verschuer, O.: Die Anlage zur Entstehung von Zwillingen und ihre Vererbung, Arch. f. Rassen-u. Gesellsch.-Biol. **26**:361, 1932.

6. Greulich, W. W.: Heredity in Human Twinning, Am. J. Phys. Anthropol. **19**:391, 1934.

of 150 mm. of mercury, quickly filled the circuit of blood vessels leading into the first cord. A yellow mass, injected into the other artery of the second cord at 250 mm. of pressure, mingled with the red mass in vessels of both parts of the placenta.

Blood Type and Physical Characters.—In blood type and physical characters, such as skin, color of hair and eyes, pattern of eyes, shape of ears, size of head and chest and body length, the twins were given the same or similar ratings (table 4). A comparison with their parents was also made. It will be noted in table 4 that both twins inherited recessive traits for blue eyes and dominant ones for lobed ears.

Dermatoglyphic Features.—The twins were palm printed and sole printed in the hospital at 8 weeks of age, from ten to twenty prints having been made of each palm and sole. Later, at 11 weeks, their finger patterns and ridge counts were read directly with a binocular microscope at a magnification of 30.

TABLE 4.—*Blood Types and Physical Characters of Twins Garry and Glen T. and Their Parents*

	Garry T.	Glen T	Father	Mother
Blood group	A (II, Jansky)	A	A	A
Skin color (Schultz)	8	8	8	8
Hair color (Schultz)	6	5 (6)	9	8
Eye color (Schultz)	2 b (blue)	2 b (blue)	1 c (blue)	8 (brown)
Pigment pattern (Hesch)	2	2	2	10
Shape of ears	Lobed	Less lobed	Lobed slightly	Adherent
Head size (inches)	14	13¾		
Chest size (inches)	12¾	13		
Length (inches)	19½	19		

The procedure of printing was to tone up the skin with 100 per cent alcohol and then to rub into it a small amount of greasy face cream. The infant's palm was then extended and held firmly by an assistant while the operator touched it lightly with a piece of highly glazed kimeograph paper held against her own hand. Several prints were made after each application of cream. The prints were later dusted with finely sifted lampblack to bring out the impression and were then fixed with resin dissolved in alcohol (30 Gm. of resin in 1 liter of 95 per cent alcohol).

Readings of the epidermal patterns were made both from the prints themselves and from enlarged photographs of these prints. Since the parents and part of the family connection were cooperative, prints and records were obtained from a number of the relatives. The same procedure of printing was followed for the adults, except that the kimeograph paper was placed on a rubber pad which could be suitably elevated with small rubber sponges to give desired pressure in the hollow of the palm and at the bases of the fingers and toes.

Finger Patterns.—In types of finger patterns and ridge counts there is close agreement between twins Garry and Glen T., comparable with that found in identical twins. Homolateral differences in ridge counts amounted to 1.5 per cent and in types of finger patterns to 10 per cent (tables 5 and 6).

Palmar Patterns.—The palmar patterns of the twins are markedly different. In both of Glen's hands, triradius D under the fifth finger is

TABLE 5.—*Finger Patterns* and Ridge Counts of Twins Garry and Glen T. and Their Parents*

	Left Fingers					Quantitative Value			Right Fingers				
	V	IV	III	II	I	Left	Total	Right	I	II	III	IV	V
Garry T.	U 0-1	U 0-3	U 0-2	A	A	6	13	7	A	U 3-0	U 3-0	U 1-0	A
Glen T.	U 0-1	U 0-2	U 0-1	A	A	4	9	5	A	U 1-0	U 3-0	W 1-1	A
Mother	U 0-6	U 0-12	U 0-8	A	U 0-5	31	63	32	U 4-0	R 0-2	U 3-0	W 14-2	U 9-0
Father	W 8-1	U 0-0	U 0-13	U 0-12	U 0-17	59	123	64	U 18-0	U 12-0	U 12-0	U 9-0	U 3-0

* Symbols: A indicates arch; U, loop ulnar; R, loop radial; W, whorl.

TABLE 6.—*Percentile Differences Between Hands of Twins Garry and Glen T. as Compared With Averages for Identical and Fraternal Twins*

	Homolateral Differences for				
	Ridge Counts of Fingers (1) %	Types of Finger Patterns (2) %	Main Lines and Axial Triradii (3) %	Palmar Patterns (4) %	Average Difference, %
Garry and Glen T.	1.5	10.0	75.0	40.0	31.6
Identical twins *	8.0	19.0	28.0	21.0	19.0
Fraternal twins *	30.0	44.0	41.5	36.5	37.9
Bilateral Differences					
Garry T.	0.0	10.0	35.0	15.0	20.0
Glen T.	1.5	10.0	0.0	0.0	2.8

* Percentile differences for identical and fraternal twins are from MacArthur and Ford (A Biological Study of the Dionne Quintuplets, an Identical Set, in Collected Studies on the Dionne Quintuplets, Toronto, University of Toronto Press, 1937).

lacking, and all main lines run to the ulnar side of the palm. The percentile difference between Garry and Glen in main lines and palmar patterns is 57.5 per cent, while for identical twins the average difference is only 24.5 per cent and for fraternal twins only 39 per cent (table 6, columns 3 and 4).

When the twins are compared with their parents in respect to main lines and palmar patterns, the closest resemblance is between Garry and his father, with a difference of 40 per cent. The patterns in Glen's hands find no counterpart in those of any member of the family group so far examined. Unfortunately, the paternal grandfather and his relatives,

estranged from the family group, refused to be part of the study. The explanation is therefore offered that since Glen during fetal development was carried in the inner sac of the membranes, in his case there was some disturbance in growth during the early fetal months which has been recorded in the patterns of his epidermal ridges. A striking instance of such recorded disturbance is found in the palmar patterns of mongoloid imbeciles (Cummins,[7] Workman [8]). Cummins [9] also recorded a case of monochorionic twins (so diagnosed by Schultz) with palmar

TABLE 7.—*Plantar Formulas of Twins Garry and Glen T. and Their Parents*

	Left Sole	Right Sole
Garry T.	7.5.5.5.5/13.-O.O.O.D^{d}.O.O.I^{d}.	7(8).5(6).5.5.13.-O.O.O.I^{d}_{d}.O.O.I^{d}.
Glen T.	7.5.5.5.13.-O.O.O.I^{d}_{d}.O.O.I^{d}.	8.6.5.5.13.-O.O.O.I^{d}_{d}.O.O.I^{d}.
Father	7.5.5.5.5.-O.O.O.A.O.O.I^{d}.	7.5.13.5.5.-O.O.O.A.I^{p}.O.I^{d}.
Mother	15.15.0.15.13.-O.O.O.I^{d}.O.O.O.	15/13.9.0.7.13.-O.O.O.I^{d}.O.I^{d}.O.
Paternal grandmother	7.5.5.15.13.-O.O.O.I^{d}_{d}.O.O.I^{d}.	7(8).6.5.5/15.13.-O.O.O.I^{d}_{d}.O.O.I^{d}.

TABLE 8.—*Percentile Differences Between Hands and Soles of Twins Garry and Glen T. and Their Parents*

	Homolateral Differences for					
	Ridge Counts of Fingers (1) %	Types of Finger Patterns (2) %	Main Lines and Axial Triradii (3) %	Palmar Patterns (4) %	Plantar Patterns (5) %	Average Difference, %
Garry-Glen	1.5	10	75	40	6.2	26.5
Garry-father	42	55	40	40	30	41.4
Garry-mother	18.1	50	85	60	61.2	64.8
Glen-father	43.5	60	80	70	32.2	57.1
Glen-mother	19.6	50	100	50	56.2	55.1
Father-mother	23.8	35	75	75	80	57.7
Father-paternal grandmother	3.7	20	50	55	40	42.2

patterns so different that on the basis of these patterns alone the twins would have been classified as fraternal.

Plantar Patterns.—In plantar configurations the twins are similar, with a percentile difference of 6.25 (tables 7 and 8), an amount con-

7. Cummins, H.: Dermatoglyphic Stigmata in Mongolian Idiocy, Anat. Rec **64** (supp.):11 (March) 1936; **73**:407, 1939.

8. Workman, G.: A Study of the Palmar Dermatoglyphics of Mongoloid Idiots, Thesis, University of Toronto School of Graduate Studies, 1939.

9. Cummins, H.: Dermatoglyphics in Twins of Known Chorionic History, with Reference to Diagnosis of the Twin Varieties, Anat. Rec. **46**:179, 1930.

sistent with monozygotic twinning. When the difference in plantar patterns is averaged with the difference in the patterns of the palms (table 8) the difference between the twins is reduced to 26.5 per cent.

Evidence of Monozygosity.—All the evidence examined, except that of the palmar patterns, points to a monozygotic origin of the twins. It is therefore concluded that the pair are uniovular and that the twin which was carried within the inner amnion had been subjected to a developmental handicap which was recorded in his palmar patterns.

CASE 2 (Robert and Richard G.).—On April 8, 1939, a 21 day old baby (Robert G.) was admitted to the hospital. The history given by the parents was to the effect that the child had begun vomiting in projectile fashion three days prior to admission, that the vomiting had occurred directly after each feeding and that since its onset the child had lost weight.

The parents were healthy, aged 23 and 24 years, and this child, 1 of twin boys, had been born after a normal pregnancy and labor. The baby's birth weight was 5 pounds 3 ounces (2,341 Gm.); the weight on admission was 4 pounds 12 ounces (2,107 Gm.).

Physical examination revealed a poorly developed and nourished child who was acutely dehydrated. There was no evidence of infection. The abdomen was distended, and visible peristaltic waves could be seen passing across the upper portion of the abdomen from left to right. A small, firm tumor was palpated in the right upper quadrant.

Treatment consisted of the administration of fluids intravenously and interstitially, followed by a small transfusion of whole blood. On April 11 operation was performed. A small, firm pyloric tumor was found, and the muscle fibers were split in the usual fashion.

The postoperative condition was poor. The child persistently refused or vomited his feedings. On April 13 the first evidence of infection appeared with a mild injection of the right ear drum. Treatment was instituted for the otitis media, but the following day the child was breathing irregularly and was cyanotic, and in spite of oxygen and stimulants he died on the evening of April 14.

At autopsy, the site of operation was found to be healing satisfactorily. Acute right otitis media and a blood culture positive for hemolytic streptococcus were the only abnormal findings.

On April 11, the day on which his twin had his operation, the second member of this pair of twins (Richard G.) arrived at the hospital with a history of projectile vomiting of three days' duration. This twin's birth weight had been 5 pounds 8 ounces (2,463 Gm.), and his weight on admission was 5 pounds 5 ounces (2,390 Gm.).

The same visible peristalsis and palpable tumor were present in this child as in his brother. He was not dehydrated, and a successful Ramsted operation was performed on April 12. This infant made an uncomplicated recovery, gained 17 ounces (414 Gm.) during his stay in the hospital and was discharged on May 2, completely well.

DETERMINATION OF TYPE OF TWINNING OF ROBERT AND RICHARD G.

Since the examination of the physical features of Robert and Richard G. was not made until after the death of 1 of the infants, the comparisons are necessarily incomplete, although the following records were obtained.

General Appearance.—In general appearance the twins resembled each other closely and were described as "identical" by members of the hospital staff. This general impression was borne out in the following physical features, for which the twins were given the same rating: color of hair by the Schultz chart, 5; eyelashes, medium in length, sandy; eyebrows, medium in extent, fair; hair form, straight; hair whorl, clockwise; nose, very broad across tip; ears, with free lobule of medium length and helix forming a wide roll.

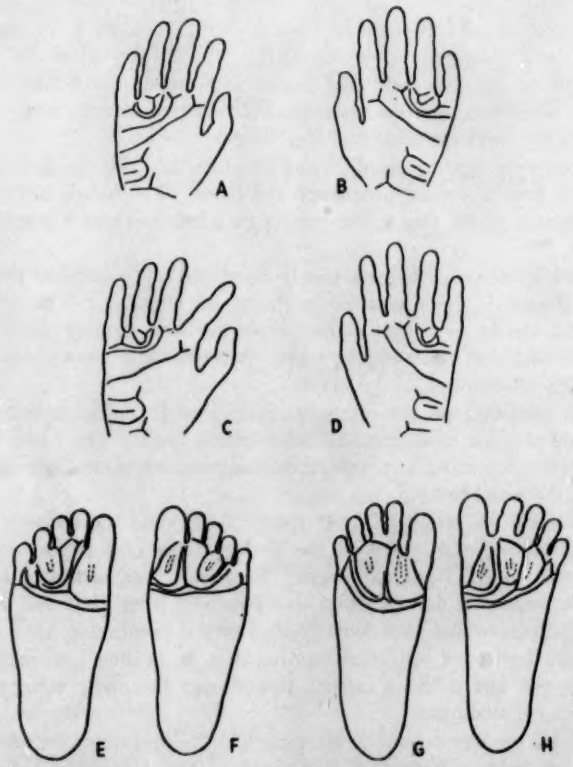

Fig. 2.—Outlines of the palmar and plantar configurations of Robert and Richard G. *A, B* are palmar, *E, F* are plantar patterns of Robert. *C, D* are palmar, *G, H* are plantar patterns of Richard.

Blood Type and Bodily Measurements.—The blood group for each twin was A (type II, Jansky). In bodily measurements the amount of difference between the infants was within the range found to obtain for identical twins generally.

	Robert	Richard
Birth weight	5 lb. 3 oz. (2,341 Gm.)	5 lb. 8 oz. (2,463 Gm.)
Size of head	13½ in. (34.3 cm.)	13 in. (33 cm.)
Size of chest	12 in. (30.5 cm.)	11 in. (28 cm.)
Length	18½ in. (47 cm.)	19 in. (48.3 cm.)

Birth Membranes.—The placenta, as described by Dr. A. E. H. Couch, was single, with two cords. Amniotic fluid was discharged only once, and hence the membranes were probably monochorionic and diamniotic.

Dermatoglyphic Patterns.—The palms and soles of the twins were printed in the hospital, and their finger patterns were also recorded by direct readings. Prints of Richard were rechecked in August 1939. Outline drawings of the palmar and plantar patterns are given in figure 2; their formulations, in table 9.

TABLE 9.—*Finger Patterns and Palmar and Plantar Formulas of Twins Robert and Richard G.*

	Robert G.	Richard G.
Finger patterns (Digits I-V)		
Left hand	U . W . U . U . U .	W . U . U . W . U .
Right hand	W . W . U . W . U .	W . W . W . W . U .
Palmar formulas (Cummins, H., and others: Am. J. Phys. Anthrop. **12**: 415 [Jan.-March] 1929)		
Left palm	9(8).7(6).5″.5′-t′t″-L^a/A^c.O.O.O.L.	9.7.5″.5′(4)-t′t″-L^a/A^c.O.O.O.L.
Right palm	9.7.5″.5′-tt″-L^a.O.O.O.L.	9(8).7(6).5″.5′-tt″-L^a.O.O.O.L.
Plantar formulas (Wilder, H. H., and Wentworth, B.: Personal Identification, Chicago, T. G. Cooke, 1932)		
Left sole	A Q U O dd	A O U O d
Right sole	A O U O d	A U U O dd
Plantar formulas (MacArthur and Ford, 1937)		
Left sole	15.9.7.7(15/7).13-O.O.O.L^d.O.L^d.L^d.	15.9(15/9).0.15(15/7).12-O.O.O.L^d.O.L^d.O.
Right sole	15.10.7(8).0.13-O.O.O.L^d.O.L^d.O.	15.15/10.15/8.0.13-O.O.O.L^d.L^d.L^d.O.

Finger and Palmar Patterns.—Ridge counts, which were fairly high in number, could not conveniently be made for the deceased infant; so only finger patterns have been recorded. The latter show a homolateral difference in four pairs of fingers, an amount of difference consistent with monozygotic twinning (Stocks[10]).

A comparison of the palmar dermatoglyphic patterns of the twins shows only slight differences in both the line terminations and the patterns. Homolaterally the difference in the main lines is 12.5 per cent.

The homolateral difference for finger and palmar patterns together is 17.5 per cent, an amount within the range found to obtain for identical

10. Stocks, P.: A Biometric Investigation of Twins and Their Brothers and Sisters, Ann. Eugenics **4**:49, 1930.

twins generally (22.6 per cent) and at variance with the greater difference in fraternal twins (40.6 per cent) (table 10).

The bilateral difference for each twin is greater than the homolateral (20 and 21.6 per cent as compared with 17.5 per cent, table 10), complying thus with the generally accepted criterion for monozygotic twinning referred to in case 1.

Plantar Patterns.—The plantar patterns exhibit bilateral low grade syndactyly in both twins, the partial fusion of the second and third digits being clearly marked in the arrangement of the dermal ridges which bind these two toes together at their bases. Syndactyly of this type is present in approximately 35 per cent of persons. (This statement is based on a study of 270 subjects selected at random.) In such syndactyly it is frequently found that one or the other of the two digital triradii which are involved may be absent. This variation increases consid-

TABLE 10.—*Percentile Differences Between Hands of Twins Robert and Richard G. as Compared with Averages for Identical and Fraternal Twins*

	Homolateral Differences for			
	Types of Finger Patterns (2) %	Main Lines and Axial Triradii (3) %	Palmar Patterns (4) %	Average Difference, %
Robert and Richard G.	40.0	12.5	0.0	17.5
Identical twins	19.0	28.0	21.0	22.6
Fraternal twins	44.0	41.5	36.5	40.6
	Bilateral Differences			
Robert G.	40.0	15.0	5.0	20.0
Richard G.	40.0	20.0	5.0	21.6

erably both the bilateral and the homolateral differences in twins who are syndactyloid. Twins Robert and Richard G. are a case in point, their homolateral difference amounting to 25 per cent and their bilateral difference to 27.5 per cent (Robert) and 40 per cent (Richard).

Evidence of Monozygosity.—All the evidence assembled (description of birth membranes, physical measurements, blood grouping and dermatoglyphic patterns) indicates that twins Robert and Richard G. were a monozygotic set.

MONGOLOID STIGMAS IN THE PALMAR DERMATOGLYPHIC PATTERNS OF TWINS ROBERT AND RICHARD G.

On each palm of twins Robert and Richard G. a somewhat unusual pattern was found in the hypothenar area. This pattern is in the form of a loop opening to the ulnar side and is recorded in the palmar formula as Lu (figs. 2 *A* to *D*, table 9). It has been shown by Cummins [9] and confirmed by Workman [8] that this particular pattern is the commonest

type seen in the palms of mongoloid imbeciles but that it is infrequent in the palms of normal persons (occurring in over one third of the palms of mongoloid imbeciles as against about one fiftieth of the palms of normal persons). It is believed that such a pattern results from a disturbance of growth which was in progress during the third and fourth fetal months, for at that time the epidermal ridges are laid down and their development completed.

The presence of these palmar patterns in twins Robert and Richard G. suggests that they bore a double handicap, that is, some disturbance of growth in addition to the abnormality of pyloric stenosis.

SUMMARY

The condition of pyloric stenosis is described in 2 pairs of male twins.

In spite of the marked differences in the palmar patterns of 1 pair, Garry and Glen T., it is concluded, on the basis of all the other evidence available, that the twins are of monozygotic origin.

The placenta of the twins mentioned is described as having one amnion enfolded within the other. It is suggested that the unusual arrangement of these fetal membranes may have caused a disturbance in the growth of the embryo contained in the inner sac, which disturbance is recorded in the palmar patterns of Glen.

The second pair of twins, Robert and Richard G., were undoubtedly a monozygotic set.

The presence of a mongoloid stigma in the palmar patterns of the second pair of twins records a disturbance of growth in the early fetal months and suggests that a double handicap was borne by these twins, 1 of whom died three days after operation.

Nine additional sets of twins, in which 1 member had pyloric stenosis, were found to be fraternal.

Twinning as an etiologic factor in pyloric stenosis is suggested, since more than twice the expected number of twins were included in 436 patients with the abnormality (1 in 36.3).

AMEBIASIS IN INFANTS AND IN CHILDREN

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The statement occurs in some of the standard textbooks of pediatrics and in reports of surveys of amebic dysentery that amebiasis in infants and children is exceedingly rare, except in the tropics. That this belief is current in children's hospitals is manifested by the surprise and incredulity frequently expressed when the presence of Endamoeba histolytica in a patient's stools is reported by the laboratory and by the pediatrician's questioning attitude as to its significance. We were cognizant of this statement in the literature and of its rather general acceptance. We remembered that since the Chicago epidemic of amebic dysentery Spector [1] had made several surveys of amebiasis in children's institutions, and Nichamin and his associates [2] had made one. Knowing that there had been a few patients with amebiasis in Sarah Morris Hospital in recent years, we became interested in compiling the references on surveys of amebiasis in infants and children and in studying the records of our patients who had amebiasis.

We are reporting the results of our study because: (1) the incidence of amebiasis indicates that infection with the parasites is definitely not rare in children, (2) several of our patients had abdominal symptoms simulating those of acute appendicitis and (3) E. histolytica was proved to be the agent causing such symptoms as vague abdominal discomfort, malaise and slight elevation of temperature, in several undernourished children, since the patients promptly improved after treatment for amebiasis was instituted.

There were certain advantages in making a survey of amebiasis among the infants and children in Sarah Morris Hospital; an extensive survey of amebiasis had already been made in the adult division of the

This study was aided by a grant from the A. B. Kuppenheimer Fund.

From the Department of Bacteriology and Parasitology of the Nelson Morris Institute for Medical Research of Michael Reese Hospital.

1. Spector, B. K.: Amebiasis in Chicago, Am. J. Pub. Health **27**:694-700 (July) 1937.

2. Nichamin, S. J.; Poncher, H. G., and Hood, M.: Amebiasis in Children, J. Pediat. **5**:741-749 (Dec.) 1934.

hospital,[3] and therefore an unusual opportunity was presented for the same personnel, using identical methods, to compare the incidence among the children with that among adults who were of the same social and economic levels. Some of the children found to have amebiasis were admitted to the children's hospital from the clinic and on discharge were referred back to the clinic. It was possible, therefore, to follow these children's course in regard to such points as treatment, recurrences, reinfections, and family contacts. It was also possible through the social worker to learn the children's family backgrounds and their histories over a course of years.

The reports of investigators on the incidence of amebiasis in infants and children are somewhat contradictory. Holt and Howland [4] made the statement that amebiasis in children is rare in this country, while Griffith and Mitchell [5] reported that tropical dysentery, caused by E. histolytica, may occasionally be encountered in the temperate zone. Harris,[6] in 1898, stated that amebiasis is infrequent in children and put the ratio at 1 child infected to every 10 adults who acquire the disease. Strong,[7] in 1898, in recording the case of a 3 year old child, reported that though amebiasis is comparatively rare it occurs throughout the United States. On the other hand, in Osler's "Modern Medicine" [8] one reads that the disease is common in this country and in children under 10 years of age, and Archer [9] warned that the incidence of amebic dysentery is increasing and recommended more detailed study of the various types of diarrhea. Although there has been this difference of opinion with regard to the prevalence of amebic dysentery in children, most authorities have expressed the belief that complications are less frequent in children than in adults. Sweet [10] noted that even in the tropics abscesses of the liver

3. Howell, K.: Incidence of Amebiasis, Typhoid and Dysentery in a Chicago Hospital, Proc. Inst. Med. Chicago **12**:193-196 (Nov. 15) 1938.

4. Holt, L. E., and Howland, J.: Diseases of Infancy and Childhood, New York, D. Appleton and Company, 1927, p. 304.

5. Griffith, J. P. C., and Mitchell, A. G.: The Diseases of Infants and Children, Philadelphia, W. B. Saunders Company, 1933, p. 590.

6. Harris, H. F.: Amoebic Dysentery, Am. J. M. Sc. **115**:384-413 (April) 1898.

7. Strong, L. W.: Two Cases of Amoebic Enteritis, M. & S. Rep. Boston City Hosp., 1898, pp. 249-259.

8. Strong, R. P.: Amoebic Dysentery, in Osler, W.: Modern Medicine, Philadelphia, Lea Bros. & Company, 1907, vol. 1, chap. 22, p. 490.

9. Archer, J. G.: The Increasing Incidence of Amoebic Dysentery as a Warning for More Study of Diarrheas, New Orleans M. & S. J. **85**:418 (Dec.) 1932.

10. Sweet, L. K.: Amoebic Abscess of Liver: Report of a Case in a Child Five Years Old, J. Pediat. **5**:750-755 (Dec.) 1934.

are rare in children though they are common in adults. However, he mentioned Brown's report in 1824 of a case of abscess of the liver in a 1 year old child. (The diagnosis was made later from the recorded description of the case.) Craig and Faust [11] reported that age has a marked influence on the incidence of amebiasis in children; the lower incidence in younger children is due to their lesser chance of exposure to the infection. Musser [12] stated that amebiasis is a disease of adult life and is rarely contracted before the age of 10 years, that in fact it is a clinical curiosity in childhood.

In view of the rather universal belief that complications are not common in children with amebiasis, it is interesting to note that some of the earliest cases recorded in children were diagnosed from abscess of the liver. For example, Dobell,[13] in England, on the basis of old pathologic records, reported the occurrence of an abscess of the liver in a child 3½ years old in 1881. Slaughter,[14] in 1895, reported the case of a 7 year old child in this country who had hepatic abscess, and Niblock [15] reported the case of an 11 month old Hindu child with a tropical abscess of the liver and stated that 3 other children in the family died of the same complaint.

Table 1 contains data from a number of surveys that have been made on infection with E. histolytica in infants and children. The surveys were selected to illustrate the distribution of amebiasis in children throughout the United States and to compare the incidence of amebiasis in different climates. A comparison of the percentages obtained from different surveys of amebiasis is always somewhat unsatisfactory because of the different methods employed by the various investigators. For example, the number of children examined varied from a few to hundreds, which, of course, affected the incidences obtained. One observer may base his results on a single fecal examination, while others use several examinations; it is an established fact that the more specimens examined, the higher is the percentage of infections detected. One worker may base his diagnosis on wet smears only, while others use

11. Craig, C. F., and Faust, E. C.: Clinical Parasitology, Philadelphia, Lea & Febiger, 1937, p. 47.

12. Musser, J. H.: Amebiasis, Am. J. M. Sc. **174**:1-8 (July) 1927.

13. Dobell, C.: A Report on the Occurrence of Intestinal Protozoa in the Inhabitants of Great Britain with Special Reference to E. Histolytica, Medical Research Council, Special Report Series, no. 59, London, His Majesty's Stationery Office, 1921.

14. Slaughter, R. M.: Abscess of the Liver in Children with Report of One Case of Amoebic Liver Abscess, Virginia M. Monthly **22**:722-731 (Oct.) 1895.

15. Niblock, W. J.: Infantile Hepatic Abscess, Indian M. Gaz. **46**:134-137 (April) 1911.

cultures and smears. The age groups of the children were also different in the surveys studied. However, in spite of the diversity of standards, it is obvious from the data in table 1 that infection of children with

TABLE 1.—*Results of Surveys of Infections with E. Histolytica in Infants and Children*

Observer	Locality	Year	Age of Subjects, Yr.	Percentage Infected
Dobell [13]	Great Britain:			
	Sheffield	1919	Under 17	5.3
	Bristol	1921	Under 12	2.0
	Leeds	1921	Under 12	1.6
	Liverpool	1921	Under 12	1.8
Boeck, W. C.: J. Parasitol. **7**: 191 (June) 1921	Industrial School for Boys and Girls	1921	Not recorded	10.8
Faust, E. C.: Am. J. Hyg. **11**: 371-384 (March) 1930	Southwestern Virginia	1930	1 mo. to 5 yr.	16.5
		1930	6 to 15	20.0
Meleney, H. E.: J. Parasitol. **16**: 146-153 (March) 1930	Tennessee	1930	Under 17	17.3
Milam, D. F., and Meleney, H. E.: Am. J. Hyg. **14**: 325-336 (Sept.) 1931	Rural Tennessee	1931	Under 4	20.7
		1931	5 to 9	35.0
		1931	10 to 14	38.0
		1931	15 to 19	45.5
Faust, E. C.: Am. J. Trop. Med. **11**: 231-237 (May) 1931	Panama River Village A	1931	1 to 5	35.0
		1931	6 to 15	90.9
	Panama River Village B	1931	1 to 5	32.8
		1931	6 to 15	30.0
	New Orleans clinics	1931	6 to 15	7.7
	New Orleans boys' home	1931	6 to 15	12.5
Daugherty, M. S.: Am. J. Trop. Med. **13**: 317-325 (May) 1933	13 southern cities	1933	Under 15	8.0
Nichamin, Poncher and Hood [2]	Departments of pediatrics and internal medicine, University of Illinois College of Medicine	1934	7 to 12 (6 patients)	Not recorded
Spector [1]	Chicago: Cook County Children's Hospital	1934	Not recorded	4.8
	Children's Memorial Hospital and Home for Crippled Children	1934	Not recorded	4.4
	Country Home for Convalescent Children	1936	10 to 16	5.5
Owen, W. B.; Honess, R. F., and Simon, J. R.: J. A. M. A. **102**: 913-915 (March 24) 1934	St. Stephens Mission School for Indian Children, Wyoming	1934	Not recorded	26.5
Summerlin, H. S.: J. A. M. A. **102**: 363-364 (Feb. 3) 1934	San Diego, Calif.	1934	Not recorded	0.4
Howell and Knoll: Present report	Sarah Morris Hospital, Chicago	1939	1 to 14	3.1
Miller, M. J.: Canad. M. A. J. **41**: 120-124 (Aug.) 1939	Orphan Asylum, Saskatchewan, Canada	1939	2-5 to 18	23.4
Spector, B. K.; Hardy, A. V., and Mack, M. G.: Pub. Health Rep. **54**: 1106-1113 (June 23) 1939	Albuquerque Indian School:			
	Pueblo	1939	10 to 16	25.6
	Navajo	1939	10 to 16	29.0
	New Mexico	1939		
	Indians without acute diarrheal disease		Under 5	8.6
	Indians without acute diarrheal disease		5 to 14	30.4
	Non-Indians without acute diarrheal disease		Under 5	7.9
	Non-Indians without acute diarrheal disease		5 to 14	12.4
Howell and Knoll: Present report	Orphanage, Chicago	1940	Under 14	4.8

E. histolytica is not rare, and that it occurs throughout the United States in all climates and in both rural and urban populations. The incidence tends to be higher in tropical regions than in other localities.

MATERIAL AND METHODS

The present report is based on study of the 18 children with amebiasis admitted to Sarah Morris Hospital from 1929 (the date of the first case of amebiasis in a child recorded in Sarah Morris Hospital) to 1940. Fecal specimens were not solicited for examination, but those sent to the laboratory for bacterial culture, for parasitic examination or for both were studied. The technic employed in examining the stools for E. histolytica was essentially that established by the laboratories of the Chicago Board of Health in 1933. Freshly passed stools were brought to the laboratory in sealed half-pint paper cartons or occasionally in a diaper. The specimens were placed in the incubator at 37 C. and examined as soon as possible. The routine examination for amebic cysts and trophozoites consisted of two moist smear examinations—one in physiologic solution of sodium chloride and one in compound solution of iodine—and a culture. The culture medium employed was a liver infusion agar slant overlaid with blood serum diluted with 6 parts of physiologic solution of sodium chloride, to which a small quantity of sterile rice powder had been added (Cleveland's medium[16]). If the fecal specimen in any way suggested the presence of E. histolytica by its gross or its microscopic appearance or by the presence of other parasites, another specimen was requested. Subsequent surveys indicated that by these procedures the amebas were detected in a high percentage of the stools which contained them in the initial survey.

TABLE 2.—*Incidence of Infection with E. Histolytica Among Children Admitted to Sarah Morris Hospital*

	Year			
	1937	1938	1939	Total
Number of children examined	121	158	129	408
Number infected	5	3	5	13
Percentage infected	4.17	1.88	3.88	3.18

Identical specimens of feces were cultured for bacteria of the typhoid-dysentery groups according to standard methods. None of the stools containing E. histolytica had bacteria of these groups.

We based the incidence for amebiasis among the infants and children admitted to Sarah Morris Hospital on the rate of occurrence among the children during the three years for which complete records were available—1937, 1938 and 1939. The data obtained appear in table 2.

OBSERVATIONS

Of the 408 children and infants who were examined, 13, or 3.18 per cent, were infected. During the same period, 1,044 adult patients were examined, of whom 55, or 5.2 per cent, were found to have amebiasis. This percentage is considerably higher than that obtained for the children, an observation reported by many investigators. Since the stools of the

16. Cleveland, L. R., and Collier, J.: Various Improvements in Cultivation of Endamoeba Histolytica, Am. J. Hyg. **12**:606-613 (Nov.) 1930.

adults and those of the children were examined by the same workers during the same period and since identical methods for the detection of E. histolytica were used, the percentages for the two groups are comparable.

The year of admission, the age incidence and the form of E. histolytica harbored on admission by each of the 18 hospitalized children appear in table 3. It is clear from the examination of the data in table 3 that children of any age can become infected with E. histolytica. The ages of the children in this study varied from 8 months to 13 years. The 8 month old infant had had severe diarrhea at the age of 2 months, but the stools

TABLE 3.—*Data for Eighteen Patients Infected with E. Histolytica*

Year	Patient	Age, Years	Form of E. Histolytica Found at First Examination	
			Cysts	Trophozoites
1929	1	7½	+	—
1931	2*	7½	+	—
1934	3*	13	—	+
1936	4	5	—	+
1936	5*	10	—	+
1937	6	6	+	+
1937	7*	8	+	+
1937	8*	8 mo.	—	+
1937	9	4	—	+
1937	10	15 mo.	+	+
1938	11*	8	—	+
1938	12*	11	+	—
1938	13*	7	+	+
1939	14*	12	+	+
1939	15	12	+	—
1939	16	9	+	—
1939	17	10	—	+
1939	18	12	—	+

* The patient was admitted to the hospital more than once, because of amebiasis or other disease.

were not examined at that time; so it is impossible to state whether amebiasis was the cause of the diarrhea. The first child with amebiasis treated in Sarah Morris Hospital was admitted in 1929, followed by 1 in 1931, 1 in 1934, 2 in 1936, 5 in 1937, 3 in 1938 and 5 in 1939. The illnesses of 2 of these children occurred before the Chicago epidemic, and those of 16, after the epidemic. Our results agree with those of Archer,[9] who in 1937 reported that his records indicated that the actual incidence of amebiasis in children was increasing and that in addition improvement in the method of culture of E. histolytica had increased the percentage of positive findings. Twelve of the 18 children infected with E. histolytica were boys, and 6 were girls. The number is too small to warrant any conclusion as to sex distribution, but the observation is in accord with that of other investigators, who have almost uniformly found a higher incidence of infection with E. histolytica in males than in females.

The 18 children were admitted to the hospital with various complaints. Some had a history of "colitis" or of repeated intestinal upsets occurring over a period of years. A number had acute abdominal pains, nausea and fever, and others had no gastrointestinal symptoms at all and were admitted for other reasons. For example, 2 were admitted for fractures, 1 for pseudohypertrophic muscular dystrophy, 1 for inguinal hernia, 1 for removal of tonsils and adenoids, 3 with symptoms of infection of the upper respiratory tract and 1 because of eosinophilia (60 per cent). Several "contacts" were hospitalized for examination because other members of the family had amebiasis. However, whether a child was admitted because of acute abdominal distress or because of other complaints, a careful history and physical examination almost always revealed that the patient had had acute abdominal pain—usually cramp-like—nausea, vomiting and intermittent attacks of diarrhea, of varying severity. Several of the children had symptoms so typical of acute appendicitis that only the early isolation of active amebas prevented operation.

On physical examination the majority of the children did not appear acutely ill, but they were nervous, anemic and undernourished. Their physical development was retarded, and in some instances their mental development was below normal. The temperatures ranged from 99 to 101 F. The blood picture confirmed the impression of anemia, since the red cell counts were between 3,000,000 and 4,000,000 and the hemoglobin content was between 60 and 70 per cent. The white cell counts were within normal limits, both in number and in distribution, except when there were such conditions as infection of the upper respiratory tract or eosinophilia. (Eosinophilia in the 1 child who had it was apparently familial, since 2 other children in the family also had high eosinophil counts.) For patients whose infection was uncomplicated by other disease, the results of urinalysis were normal. The typical stools were dark brown and unformed. In the diarrheal state pus, blood and occasionally mucus appeared.

Three case reports are sufficient to illustrate the types of amebiasis that were encountered in the children examined for E. histolytica.

REPORT OF CASES

CASE 13.—*Amebiasis in a carrier who had no symptoms.*

J. D., aged 7 years was admitted to the hospital in 1938, in an attempt to confirm by biopsy a diagnosis of pseudohypertrophic muscular dystrophy. In the course of a thorough physical examination, a fecal sample was examined. Cysts and precysts of E. histolytica were found by direct examination, and active vegetative forms, by culture. He received a course of treatment for amebiasis, and results of examinations of the stools were negative for all forms of E. histolytica before he left the hospital.

The medical social worker reported that there were 10 other children in the family in addition to the parents and that the home conditions indicated a fair degree of cleanliness in spite of poverty. The family lived at such a distance from the hospital that it was impossible to obtain fecal specimens from the entire family, but three specimens examined by us contained E. histolytica. The board of health, we understand, examined and treated the other members of the family for amebiasis.

According to the history obtained from his mother, our patient had never been subject to gastrointestinal upsets, and at no time had there been the slightest degree of abdominal tenderness. In brief, the child apparently had no symptoms referable to amebiasis and was the only one of our patients in whom the so-called host-parasite equilibrium had been established. This patient has had four subsequent admissions to the hospital for physical examination to check up on the treatment for pseudohypertrophic muscular dystrophy. On none of these occasions has E. histolytica been found in the stools, although other parasites have been occasionally observed.

CASE 6.—*Amebiasis in a carrier who had occasional exacerbations of the infection.*

S. A., a boy 6 years of age, was admitted on Aug. 18, 1937. He was brought to the hospital for observation because he complained of weakness, dizziness and poor appetite and because he had gained only 1 pound (454 Gm.) within two years. According to the history given by his mother, he had had measles, his tonsils and adenoids had been removed and he had been operated on for an infected cervical lymph gland. His mother said that he had had chills and fever at irregular intervals, with occasional attacks of vomiting and diarrhea. Physical examination revealed an anemic and undernourished child, small for his years. Study of his blood revealed hypochromic normocytic anemia. In a stool sent to the laboratory just before his discharge from the hospital, cysts of E. histolytica were found by indirect examination, and trophozoites, by culture. He was recalled to the hospital, amebas were again found and he was treated for amebiasis. Two weeks after treatment he was discharged from the hospital again as improved. Results of examination of the stools had been negative for E. histolytica on several occasions.

The child was readmitted to the hospital on August 20 of the following year. The symptoms were chills, fever (temperature 104 F.), headache, vomiting and diarrhea. Specimens of the stools were sent to the laboratory for examination and were found to contain pus, blood and cysts of E. histolytica. He was treated for amebiasis, and within thirty-six hours the diarrhea was controlled. After a course of treatment examination again revealed the stools were negative for E. histolytica, and he was discharged from the hospital again as improved.

CASE 3.—*Acute amebiasis.*

M. M., a boy aged 13, was admitted to the hospital on July 17, 1934. He had been in a boys' camp, and according to the information obtained from his mother and from a letter sent by the camp physician, he had been in good health until July 12. On that morning he reported to the camp physician that he had been ill during the night with abdominal pains and frequent attacks of vomiting. His temperature was 99.2 F. There were no physical abnormalities, and he apparently responded to treatment. However, that evening his temperature rose to 102.6 F., and the next day he had a chill, followed by a rise of temperature to 104.8 F. The nausea continued, with occasional attacks of vomiting, and he had six to eight semiliquid stools per day. The physical findings were still almost normal. There were

slight abdominal distention and muscle spasm, but too little to account for the pain and the high temperature. His parents were notified of his illness, and he was removed from the camp hospital and brought to Sarah Morris Hospital on a stretcher.

He appeared acutely ill and avoided all movement because it increased abdominal pain. In brief, he was so acutely ill that a physical examination was postponed. Examination of his blood revealed 4,700,000 red cells and 15,000 white cells, with an increase in polymorphonuclear leukocytes; the hemoglobin content was 85 per cent. A blood culture was negative for bacteria. Specimens of stools were examined for bacteria and parasites. No organisms of the typhoid-dysentery groups were present, but by direct examination numerous motile vegetative forms of E. histolytica were observed. Treatment for amebiasis was instituted; the symptoms rapidly disappeared, and examinations of the stools for trophozoites, precysts and cystic forms of E. histolytica gave negative results. The patient was discharged from the hospital on August 1, cheerful, comfortable and apparently in perfect health.

It was impossible to trace the source of infection in this patient. No other member of the camp was affected. On a subsequent admission, a year later, no form of E. histolytica could be found in the boy's stools, although a number of examinations were made.

COMMENT

Under treatment the symptoms of amebiasis cleared up quickly in all the children. The first 2 patients, whose illnesses occurred in 1929 and 1931, were treated with emetine hydrochloride, and the others with carbarsone. Stools became persistently negative for the parasites after one or two courses of treatment. Some of the children had several admissions to the hospital during the eleven year observation period; sometimes they entered with symptoms of amebiasis and sometimes with symptoms of totally different diseases. Even in the latter instances E. histolytica was frequently found in the stools. Since no child who harbored E. histolytica was ever discharged from the hospital before there was marked clinical improvement and before frequent and successive examinations of fecal specimens were negative for all forms of E. histolytica, and since there was a lapse of time between admissions, it seems probable that reinfection occurred, especially since other members of some of the families were known to be amebic carriers. The readmissions suggest that the children had neither a natural immunity to E. histolytica nor an acquired immunity from the first infection. More readmissions for amebiasis occurred from the clinic group than from the children under the care of private physicians, indicating that the better standards of health in the higher social level tended to increase the resistance of the children to E. histolytica and at the same time lessened their chances of coming in contact with the parasites.

The clinical course of our patients could not be correlated with the laboratory findings if the criterion is accepted that cysts of E. histolytica in stools indicate the carrier state, with the host-parasite equilibrium

established, and that the presence of trophozoites indicates acute amebiasis. In our laboratory cysts were sometimes found in a patient's specimen one day; a few days later precysts and trophozoites were present, and other examinations disclosed all forms of E. histolytica.

We were fortunate in having an opportunity to supervise a survey of amebiasis that was conducted in a Chicago orphanage. Specimens from 105 children were examined, and in those of 5 children (4.8 per cent) E. histolytica was present. This incidence was slightly higher than that obtained in Sarah Morris Hospital. This higher percentage of infection bears out the general observation that in institutionalized groups the incidence of amebiasis is higher than in other groups.

SUMMARY AND CONCLUSIONS

Amebiasis can occur in infants and children of any age in any locality. The incidence of amebiasis has increased in children as well as in adults since 1934. Children apparently have little immunity to amebiasis, natural or acquired. Amebiasis is contracted through contact with an amebic carrier, and a low standard of living is apparently a contributing factor to infection.

The symptoms of acute amebiasis may simulate those of acute appendicitis, typhoid fever or bacillary dysentery. The symptoms of chronic amebiasis in children are occasionally atypical.

Bacteria of the typhoid-dysentery groups were not present in the fecal specimens containing E. histolytica from the children studied.

It is evident that amebiasis occurs with sufficient frequency in infants and children to warrant its consideration as a possible cause either of acute abdominal conditions or of vague, atypical gastrointestinal symptoms.

ADDIS COUNT AND FAILURE OF ORTHOTOLIDINE TEST IN CASES OF HEMATURIA IN CHILDREN

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For years we have been interested in the problems of nephritis in childhood. In the follow-up study of nephritic children the presence of continued hematuria is, among other data, of great significance. We were therefore interested in comparing several methods of detecting the presence and degree of hematuria in the patients we have seen recently.

The ordinary routine microscopic examination of the urinary sediment has the one great advantage of simplicity. The finding of red blood cells in a freshly voided specimen of urine is a valuable observation, as it is usually a definite indication of a pathologic condition in the genitourinary tract. The absence of red cells in a chance specimen needs a different interpretation. Alkaline urine quickly destroys red blood cells. Examination of a dilute specimen will often be negative for red blood cells unless sufficient time is allowed for sedimentation or the specimen is centrifuged.

In some clinics an attempt is made to determine quantitatively the number of formed elements in a specimen of urine by reporting their number per high power or per low power field. This practice, however, generally gives only an illusion of quantitative accuracy, as the result will depend on many factors: the total amount of urine in the specimen; the time allowed for sedimentation or centrifugation; the acidity of the urine; the size and depth of the drop looked at and the technic of obtaining the drop. It is well nigh impossible to keep all these factors constant all the time.

A quantitative method of studying urinary sediment was introduced in 1926 by Addis.[1] The principal purpose of this method was to eliminate the difficulties mentioned and to give comparable quantitative results. An acid, concentrated twelve hour specimen is collected. The formed elements are counted in a counting chamber. The results are reported

From the Pediatric Service of Dr. Béla Schick, Mount Sinai Hospital.

1. Addis, T.: Formed Elements in Urinary Sediment of Normal Individuals, J. Clin. Investigation **2**:409-415 (June) 1926.

as the total number of elements for the twelve hour specimen. Addis and his co-workers correlated the results with the pathologic renal conditions in their patients. They also established figures for the normal excretion of red blood cells, casts, leukocytes and epithelial cells in the healthy adult. Rew and Butler;[2] Boyle, Aldrich and their co-workers;[3] Lyttle[4] and Snoke[5] have reported on the results of the Addis count in normal and nephritic children. Snoke[6] has also established normal values for the Addis count in children: red blood cells 600,000 and casts 20,000 in twelve hours.

The Addis count is not quantitative in the strict sense of a chemical determination. However, the uniformity in collection of specimens of urine and the technic in counting the cells give results that are useful for determining clinical progress. The large dilution factor and the counting of elements in only a small fraction of the total quantity of urine are, of course, serious technical drawbacks. Yet it is the impression of most workers that a careful technic can easily be mastered and reliable and comparable results obtained.

Many simple chemical methods for the detection of blood in the urine have been devised. In these procedures the sediment is tested with one of the chemicals commonly used in the detection of blood, such as guaiac, benzidine or orthotolidine. At present orthotolidine is generally considered the best chemical for the detection of blood in urine.

The orthotolidine test for the detection of blood was first described by Ruttan and Hardisty.[7] They stated that by using a 4 per cent solution of orthotolidine in acetic acid hemoglobin in a dilution of 1 part in 7,000,000 parts of water could be detected. In urine the sensitivity of the test was much less—1 part of hemoglobin in 24,000 parts of urine

2. Rew, W. B., and Butler, A. M.: Addis Sediment Count in Children: Means of Determining Presence of Kidney Lesion, J. Pediat. **1**:216-229 (Aug.) 1932.

3. Boyle, H. H.; Aldrich, C. A.; Frank, A., and Borowsky, S.: The Addis Count in Children Following Clinical Recovery from Post-Infectious Nephritis, J. A. M. A. **108**:1496-1498 (May 1) 1937.

4. Lyttle, J. D.: Addis Sediment Count in Normal Children, J. Clin. Investigation **12**:87-93 (Jan.) 1933; Addis Sediment Count in Scarlet Fever, ibid. **12**:95-103 (Jan.) 1933.

5. Snoke, A. W.: Stages, Prognosis and Duration of Glomerular Nephritis in Childhood, Am. J. Dis. Child. **53**:673-704 (March) 1937; Prognosis of Glomerular Nephritis in Childhood, ibid. **57**:1373-1378 (June) 1939.

6. Snoke, A. W.: Normal Addis Sediment Count in Children, J. Pediat. **12**: 473-478 (April) 1938.

7. Ruttan, R. F., and Hardisty, R. H. M.: A New Reagent for Detecting Occult Blood, Canad. M. A. J. **2**:995-998 (Nov.) 1912; Ortho-Tolidin as an Indicator for Occult Blood, Biochem. Bull. **2**:225, 1913.

being necessary for a positive reaction. Stone and Burke [8] reported that the presence of approximately 1,350 red blood cells per cubic centimeter of urine results in a positive reaction to the orthotolidine test if the test is done directly on the sediment of 15 cc. of urine. Calvin and Carbone [9] again called attention to the test, in 1939. They studied children who were convalescing from scarlet fever and pointed out that the urine of 44 per cent of these children had a positive reaction to the orthotolidine test at some time during the disease. These workers concluded that the orthotolidine test was accurate for setting the limits for normal and pathologic urinary sediment with regard to erythrocytes. Barach and Pennock [10] have reported a positive result from the orthotolidine test in half of 681 adult medical patients with so-called chronic diseases. They claimed that the use of orthotolidine is a sensitive test for occult hematuria.

A simple chemical test has the advantage of even greater simplicity than the ordinary microscopic examination. Most authors have attributed a degree of quantitative accuracy to such tests. These methods unquestionably do have some quantitative value, as the positiveness of the result is in direct proportion to the concentration of hemoglobin in the specimen. On more careful scrutiny, however, one realizes that there are many other variables which influence the quantitative significance of the results. Freshly made dilutions of red blood cells are not exactly comparable to the suspension of red blood cells in the urine. In urine there may be a loss of hemoglobin through the cell membrane. Many of the forms of red blood cells seen under the microscope probably have lost a great deal of their hemoglobin. Patients with nephritis may have secondary anemia. The urine of a nephritic patient, as regards its hydrogen ion concentration and mineral and organic constituents, differs from the urine of the normal child, and varies from patient to patient.

The result of the orthotolidine test performed on a chance specimen should have limited quantitative significance. We were interested in comparing results of the orthotolidine test with results of the Addis count. The orthotolidine test is performed on the sediment of 15 cc. of a twelve hour sample of urine. Unless this 15 cc. is always a constant aliquot of the twelve hour specimen, one should not expect much correlation with the result of the Addis count, which depends to a great extent on the volume of the twelve hour specimen.

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8. Stone, W. J., and Burke, G. T.: An Improved Test for Occult Blood, Especially in the Urine, J. A. M. A. **102**:1549-1550 (May 12) 1934.

9. Calvin, J. K., and Carbone, J.: Erythrocytes in Urinary Sediment in Health and in Disease (Scarlet Fever): Studies by the Orthotolidine Test, Am. J. Dis. Child. **57**:1035-1043 (May) 1939.

10. Barach, J. H., and Pennock, L. L.: Diagnostic Value of Occult Hematuria, J. A. M. A. **114**:640-642 (Feb. 24) 1940.

EXPERIMENTAL EVALUATION OF THE ORTHOTOLIDINE TEST

Suspensions of fresh red blood cells in various dilutions were prepared in Ringer's solution and in cell-free urine of varying hydrogen ion concentration. The sediment of the urine from a nephritic child with frank hematuria was also

TABLE 1.—*Sensitivity of Orthotolidine Test*

Number of Red Blood Cells in 1 Cc. of Ringer's Solution*	Result of Orthotolidine Test
365,000	++++
328,500	+++
32,850	++
3,285	+
328	+
33	0
3	0
None	0
7,250,000	++++

Number of Red Blood Cells in 1 Cc. of Cell-Free Urine*	Result of Orthotolidine Test		
	*p*H 6	*p*H 4	*p*H 10
360,000	+++	+++	+
290,000	+++	+++	0
253,000	+++	+++	0
217,000	+++	++	0
145,000	++	0	0
108,000	++	0	0
72,500	±	0	0
29,300	0	0	0
2,600	0	0	0
237	0	0	0
23	0	0	0

* Dilutions of red blood cells were made from a solution of red blood cells in Ringer's solution by means of standard pipets.

TABLE 2.—*Sensitivity of Orthotolidine Test in a Case of Hematuria*

Number of Red Blood Cells per Cc. of Urine*	Result of Orthotolidine Test
3,200,000	+++
1,600,000	++
800,000	+
400,000	0
200,000	0
100,000	0
50,000	0
25,000	0
None	0

* Dilutions were made by adding definite numbers of cells to definite amounts of the patient's cell-free urine.

used in various dilutions in the patient's own cell-free urine. The sensitivity of the orthotolidine test was then determined on a uniform volume of 1 cc., using 2 drops of orthotolidine and 3 drops of a solution of glacial acetic acid and hydrogen peroxide (tables 1 and 2). It will be seen that the sensitivity of this test for the detection of blood varies with the solution and the hydrogen ion concentration of the medium in which the blood is present. These results parallel those of Ruttan and Hardisty and are consistent with what one would expect with the chemical mechanism involved in this test.

Method.—Specimens of urine were collected from 7 p. m. to 7 a. m. No fluids were allowed after 4 p. m., at which time supper was given, with the quantity of fluids limited to 200 cc. The specimen of urine was examined at about 9 a. m., since the Addis count must be done within a few hours after the urine is passed. The amount of urine excreted was accurately measured.

In a graduated tube 15 cc. of urine was centrifuged for twenty minutes. Then the sediment was suspended in 1 cc. of the urine by removing 14 cc. of the supernatant fluid with a pipet. One drop was used for the Addis count. On the remainder of the specimen the orthotolidine test was performed, using 2 drops of a 1 per cent solution of orthotolidine in methyl alcohol and 3 drops of a mixture of 1 part glacial acetic acid and 2 parts hydrogen peroxide.

Calvin and Carbone[9] as well as Stone and Burke,[8] performed the orthotolidine test directly on the sediment of 15 cc. of urine. As the volume of the sediment obtained from 15 cc. of urine varies markedly from specimen to specimen and from patient to patient, we resuspended the sediment of all specimens in 1 cc. of urine. A constant volume is the only possible way of quantitatively comparing the results of the orthotolidine test with those of the Addis count. The orthotolidine test is obviously made less sensitive by dilution.

The results of the routine microscopic examinations of the urine by the hospital staff were compared with the results of the Addis and the orthotolidine test.

REPORT OF CASES

Several cases illustrate the comparative values of these three methods of examining the urine. The salient points in the interpretation of these tests are emphasized in the reports.

CASE 1.—*Hematuria following administration of sulfapyridine.*

G. S., a 5 year old child with chronic bronchiectasis and pneumonia, was given sulfapyridine by mouth. Frank hematuria developed after several days of therapy. When the routine examination of the urine gave negative results for the first time after the drug was stopped, Addis counts and orthotolidine tests yielded the following results:

Date	Number of Red Blood Cells by Addis Count	Result of Orthotolidine Test	Result of Routine Microscopic Examination
10/ 4/39.....	1,875,000	Negative	Occasional white blood cell
10/13/39.....	840,000	Negative	Occasional white blood cell
10/20/39.....	210,000	Negative	Occasional white blood cell

At a later date, the patient was again treated with sulfapyridine for a second attack of pneumonia. No frank hematuria resulted. The Addis count and orthotolidine test were again performed.

Date	Number of Red Blood Cells by Addis Count	Result of Orthotolidine Test	Result of Routine Microscopic Examination
11/10/39.....	697,000	Negative	Occasional white blood cell

The child died shortly after this last attack of pneumonia. There was no renal lesion on postmortem examination.

In this case the Addis count gave evidence that renal irritation was present for at least ten days after the usual routine examination of the urine gave normal results.

CASE 2.—*Episodes of gross hematuria.*

D. S., a 9 year old child, was admitted for study because of repeated episodes of frank hematuria unassociated with pain or hypertension. We followed this patient rather closely with Addis counts, routine examinations and orthotolidine tests.

Date	Number of Red Blood Cells by Addis Count	Result of Orthotolidine Test	Result of Routine Microscopic Examination
11/ 4/39	96,000,000	++++	Gross hematuria
11/ 6/39	119,000,000	++++	Gross hematuria
11/ 8/39	66,500,000	++++	Gross hematuria
11/10/39	1,771,000	Negative	Negative
11/13/39	61,600,000	++++	Gross hematuria
11/15/39	32,400,000	++++	Many red blood cells
11/17/39	44,800,000	++++	Many red blood cells
11/22/39	32,000,000	++++	Many red blood cells

From these procedures we found that at all times this patient had an abnormal excretion of red blood cells, which at intervals increased to frank hematuria. Results of a complete study, including pyelograms, were negative. The child had several hemangiomas, and the question of a similar lesion in the kidney was raised. The child is being followed now, and our diagnosis is still deferred.

CASE 3.—*Post-tonsillectomy reaction.*

J. T., a 15 year old boy, had been well and had had no urinary abnormalities until the winter of 1937, when a faint trace of albumin and a rare red blood cell were noted in the urine, after an attack of acute tonsillitis. In April 1938 an Addis count was done, with the following results: red blood cells 200,000; casts 40,000. At that time we could not account for the increased excretion of casts in the urine.

During the subsequent winter red blood cells and albumin were again noted in the urine after an infection of the respiratory tract. Tonsillectomy was decided on and performed in October 1939. Faint traces of albumin were present in some specimens after operation. Addis counts and orthotolidine tests gave the following results:

Date	Number of Red Blood Cells by Addis Count	Result of Orthotolidine Test	Result of Routine Microscopic Examination
10/ 6/39	4,716,800	Negative	Occasional red blood cell
11/ 4/39	4,500,000	Negative	Negative

Examination of another patient, an 8 year old girl who had fever immediately after tonsillectomy, gave the following results:

Date	Number of Red Blood Cells by Addis Count	Result of Orthotolidine Test	Result of Routine Microscopic Examination
11/20/39	1,346,400	Negative	Rare red blood cells

CASE 4.—*Periarteritis nodosa.*

This was a classic case, verified by biopsy and autopsy, in which the skin, kidneys, heart, blood vessels and lungs were involved during a two year period of illness. Examination of this child during her last admission gave the following results:

Date	Number of Red Blood Cells by Addis Count	Number of Casts by Addis Count	Result of Orthotolidine Test	Result of Routine Microscopic Examination
11/13	924,000	128,000	Negative	Occasional white blood cell; many casts
11/15	1,320,000	417,000	Negative	Occasional white blood cell; occasional red blood cell; many casts
11/29	245,000	97,000	Negative	Occasional white blood cell; many casts

CASE 5.—*Subacute bacterial endocarditis.*

The patient, a 6 year old girl, had an infection with Streptococcus viridans superimposed on rheumatic heart disease. It is interesting to observe the difference between the results of the routine examinations and those of the quantitative examinations of the urine.

Date	Number of Red Blood Cells by Addis Count	Result of Orthotolidine Test	Result of Routine Microscopic Examination
2/12/40	260,000	Negative	No red blood cells
3/27/40	760,000	Negative	Occasional red blood cells

CASE 6.—*Nephritis.*

This patient had nephritis, of two years' duration, with edema, albuminuria, hematuria and hypertension. It is interesting to note the difference between the results of the Addis counts and those of the ordinary examinations, the former method showing a significant continuous, latent hematuria, while on some occasions the routine examination gave negative results.

Date	Number of Red Blood Cells by Addis Count	Result of Orthotolidine Test	Result of Routine Microscopic Examination
1/17/40	2,130,000	Negative	Occasional red blood cells
2/13/40	6,275,000	Negative	Many red blood cells
3/27/40	2,156,000	Negative	No red blood cells

In 34 cases results of the Addis count and those of the orthotolidine test were compared. These data are shown in table 3.

TABLE 3.—*Comparison of Results of Addis Count and Orthotolidine Test in Thirty-Four Cases*

Case No.	Result of Addis Count	Number of Red Blood Cells* in 1 Cc. of Urine	Result of Orthotolidine Test
16	119,000,000	6,000,000	++++
15	96,000,000	10,650,000	++++
17	66,500,000	8,750,000	++++
22	61,600,000	3,850,000	+++
26	44,800,000	3,200,000	+++
23	36,000,000	3,650,000	++++
24	32,400,000	4,050,000	++++
27	32,000,000	3,850,000	++++
32	17,250,000	1,675,000	±
31	12,814,000	430,000	0
34	12,700,000	576,000	0
4	4,716,000	264,000	0
14	4,500,000	188,000	0
1	1,875,000	187,500	0
19	1,750,000	144,000	0
7	1,346,000	204,000	0
25	1,320,000	88,000	0
21	924,000	88,000	0
3	840,000	168,000	0
20	697,000	84,000	0
28	668,000	60,000	0
13	583,000	24,000	0
12	519,000	60,000	0
9	380,000	46,000	0
10	249,600	18,000	0
30	245,000	14,000	0
2	238,000	14,000	0
6	216,000	54,000	0
8	140,000	14,000	0
11	108,000	18,000	0
18	93,600	6,000	0
29	84,000	10,000	0
5	64,000	12,000	0
33	14,000	2,000	0

* Number of red blood cells from the sediment of 15 cc. of a specimen of urine, resuspended in 1 cc. of urine.

It will be noted that a positive result from the orthotolidine test was obtainable only with an Addis count of 17,250,000 cells. Addis, Lyttle and Snoke have accepted an excretion of 600,000 red blood cells as the upper limit of normal, and Snoke stated that a count of 500,000 to 600,000 red blood cells on successive occasions should be regarded as grounds for suspecting the presence of renal disease. Specimens showing as many as 430,000 red blood cells in only 15 cc. of urine did not give a positive reaction to the orthotolidine test with the technic described. Even if the orthotolidine test were done on the sediment of 15 cc. of urine resuspended in only 0.3 to 0.5 cc. of urine (the smallest usable volume) its sensitivity would not always be sufficient to indicate an abnormal excretion of red blood cells.

COMMENT

Both the ordinary microscopic examination of urine and the orthotolidine test are largely qualitative estimates of hematuria. For a more accurate quantitative estimate the method of Addis should be used.

It would, of course, be impractical and unnecessary to do quantitative urinalyses as a routine measure. Yet in cases in which there is suspicion of renal disease, this method gives data which are of clinical value.

The full value of the Addis count in the study of renal disease is as yet to be determined by follow-up study and correlation with pathologic renal conditions. Such questions as whether a continuously abnormal Addis count is definitely indicative of progression of acute nephritis to chronic nephritis and whether repeatedly normal Addis counts are absolute evidence of the healing of acute nephritis must await final solution by long-continued follow-up study of nephritic children.

It is important to emphasize the value of repeated Addis counts in renal disease. The clinician must remember, however, that even in severe renal disease the excretion of red blood cells may be normal at times (case 4).

CONCLUSIONS

A discussion of the relative values of various methods of examination of the urine for red blood cells is presented.

The orthotolidine test is sensitive in detecting the presence of blood in the urine. However, it is neither accurate nor reliable for the estimation of pathologic excretion of red blood cells, which is revealed by the Addis count.

The Addis count seems to be of value in the clinical and in the follow-up study, of renal disease.

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CAUSES OF PREMATURITY

II. COMPARISON OF MATERNAL HISTORIES OF PREMATURE AND OF FULL TERM INFANTS

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CINCINNATI

Maternal conditions leading to the premature delivery of infants have been studied by a number of clinicians, and we have summarized their conclusions, which have differed widely, in a previous communication.[1] In the majority of these studies the incidence of these conditions in the mothers of mature infants has not been compared with the incidence in mothers of immature infants. Furthermore, the few excellent reviews in which control groups were employed depended on retrospective surveys, that is, on the analysis of observations which were not deliberately planned for the purpose of the study. In attempting to obviate some of the errors which might occur in studies of this kind, we have interviewed all of the mothers who entered the obstetric wards of the Cincinnati General Hospital during the period of one year in order to compare, under similar conditions, the histories of mothers who bore immature infants with the histories of those whose infants were mature. Our observations have been arranged so that they may be compared with those of previous students of this subject.

PROCEDURE

A total of 2,514 women admitted to the obstetric wards of the Cincinnati General Hospital were interviewed. All of the histories were taken by one clinician (N. A. A.) in order to obviate individual differences of interpretation. The information was tabulated on punch cards, and the various data were assembled by mechanical sorting.

From the Children's Hospital Research Foundation and the Department of Pediatrics of the University of Cincinnati College of Medicine.

1. Anderson, N. A., and Lyon, R. A.: Causes of Prematurity: I. Review of the Literature, Am. J. Dis. Child. **58**:586-594 (Sept.) 1939.

DETERMINATION OF PREMATURITY

In classifying infants as premature and in differentiating between stillborn and liveborn infants, there have been followed as closely as possible the definitions of the American Public Health Association:[2]

"Birth . . . is the instant of complete separation of the entire body . . . of the child from the body of the mother . . .

"No child that shows any evidence of life after birth should be registered as a stillbirth.

"Unless gestation has advanced to the 5th month, i. e., after 120 days, the product of pregnancy need not be reported as a stillbirth.

"The term *abortion* should be reserved for the expulsion or extraction of the product of conception previous to its presumed viability, usually understood to apply to a fetus of less than 28 weeks from the assumed date of conception (6½ calendar, or 7 lunar months, at which time, in the races prevailing in the United States, the fetus will weigh 1,500 grams or 3¼ pounds and have a length of 35 centimeters or 14 inches).

"The term *early abortion* should be applied only to expulsion or extraction of the product of conception prior to the end of the first 12 weeks of pregnancy.

"The term *late abortion* should be applied to expulsion or extraction of the product of conception from the end of the twelfth week, or after development of the placenta and up to the 28th week of pregnancy.

"The term *premature labor* should apply to the delivery of a fetus capable of surviving, and as usually understood, but not absolutely limited in fact, to apply to the product of conception after 28 weeks or 6½ calendar months or seven lunar months, which in American experience will usually have a weight of 1,500 grams or 3¼ pounds and a length of 35 centimeters or 14 inches."

Of these definitions the least satisfactory is that of premature labor. The upper limits of prematurity are at least as controversial as the lower. Since we have been dissatisfied with any sharp delineation on the basis of weight, we have adopted the procedure of comparing underweight or immature infants with mature infants, and we have studied our material according to different groups arranged in terms of weight. It must, of course, be recognized that some of the infants previously classified as premature may be mature in terms of gestation, although small, and that anthropometric measurements or determinations of osseous development may be better criteria of maturity in such borderline cases.

The inclusion of twins in a group of premature infants may also be questioned. Different criteria should be established for the definition of prematurity among multiple births. The multiple pregnancies, accordingly, have been excluded from the present analysis because of

2. American Public Health Association Year Book, 1935-1936, New York, American Public Health Association, 1936, pp. 244-249.

TABLE 1.—*Distribution of 2,481 Infants by Birth Weight*

Birth Weight	Single Births		Multiple Births (Twins Only)		Total
	Live Birth	Stillbirth	Live Birth	Stillbirth	
1 lb. to 1 lb. 7 oz.	1	1	..	..	2
1 lb. 8 oz. to 1 lb. 15 oz.	2	7	1	..	10
2 lb. to 2 lb. 7 oz.	7	..	..	..	7
2 lb. 8 oz. to 2 lb. 15 oz.	2	3	..	3	8
3 lb. to 3 lb. 7 oz.	7	3	3	..	13
3 lb. 8 oz. to 3 lb. 15 oz.	9	5	4	..	18
4 lb. to 4 lb. 7 oz.	21	7	5	..	33
4 lb. 8 oz. to 4 lb. 15 oz.	49	6	10	1	66
5 lb. to 5 lb. 7 oz.	108	3	5	..	116
5 lb. 8 oz. to 5 lb. 15 oz.	141	1	6	2	150
6 lb. to 6 lb. 7 oz.	303	4	5	..	312
6 lb. 8 oz. to 6 lb. 15 oz.	381	2	4	..	387
7 lb. to 7 lb. 7 oz.	458	2	3	..	463
7 lb. 8 oz. to 7 lb. 15 oz.	357	1	..	..	358
8 lb. to 8 lb. 7 oz.	236	2	..	..	238
8 lb. 8 oz. to 8 lb. 15 oz.	164	3	..	..	167
9 lb. to 9 lb. 7 oz.	76	2	..	..	78
9 lb. 8 oz. to 9 lb. 15 oz.	30	..	..	..	30
10 lb. to 10 lb. 7 oz.	14	1	..	..	15
10 lb. 8 oz. to 10 lb. 15 oz.	5	1	..	..	6
11 lb. to 11 lb. 7 oz.	1	1	..	..	2
11 lb. 8 oz. to 11 lb. 15 oz.	1	..	..	..	1
12 lb.	..	1	..	..	1
Total	2,373	56	46	6	2,481

TABLE 2.—*Distribution of 2,373 Single Liveborn Infants by Race and Sex*

Birth Weight	White Boys		White Girls		Negro Boys		Negro Girls		Total
	No.	%	No.	%	No.	%	No.	%	
1 lb. to 1 lb. 7 oz.	..		..		..		1		1
1 lb. 8 oz. to 1 lb. 15 oz.	..		1		..		1		2
2 lb. to 2 lb. 7 oz.	4		..		2		1		7
2 lb. 8 oz. to 2 lb. 15 oz.	..		1		1		..		2
3 lb. to 3 lb. 7 oz.	2		1		..		4		7
3 lb. 8 oz. to 3 lb. 15 oz.	2		..		1		6		9
4 lb. to 4 lb. 7 oz.	5		6		2		8		21
4 lb. 8 oz. to 4 lb. 15 oz.	17		12		15		5		49
Total under 5 lb.		30.6		21.4		21.4		26.5	
5 lb. to 5 lb. 7 oz.	23		28		26		31		108
Total under 5 lb. 8 oz.		25.7		23.8		22.8		27.7	
5 lb. 8 oz. to 5 lb. 15 oz.	33		36		31		41		141
6 lb. to 6 lb. 7 oz.	68		102		61		72		303
6 lb. 8 oz. to 6 lb. 15 oz.	99		101		78		103		381
7 lb. to 7 lb. 7 oz.	135		152		93		78		458
7 lb. 8 oz. to 7 lb. 15 oz.	127		108		67		55		357
8 lb. to 8 lb. 7 oz.	91		87		35		23		236
8 lb. 8 oz. to 8 lb. 15 oz.	72		53		23		16		164
9 lb. to 9 lb. 7 oz.	34		18		14		10		76
9 lb. 8 oz. to 9 lb. 15 oz.	16		8		4		2		30
10 lb. to 10 lb. 7 oz.	8		4		..		2		14
10 lb. 8 oz. to 10 lb. 15 oz.	2		2		1		..		5
11 lb. to 11 lb. 7 oz.	1		..		..		..		1
11 lb. 8 oz. to 11 lb. 15 oz.	1		..		..		..		1
Total 5 lb. 8 oz. and above		31.7		31.0		18.8		18.6	
Grand total	740	31.2	720	30.3	454	19.1	459	19.3	2,373
Total by race		1,460				913			

(1) the entirely different weight distribution of twins as compared with that of the total series of infants (table 1) and (2) difficulties which arise in the computation of results. Mothers of twins must be counted twice; mothers of triplets, three times. Furthermore, the birth weights of the twins may differ considerably; 1 infant may be stillborn, and it may be difficult to decide whether the premature delivery of the infants is due to the twinning itself or to a complication of the pregnancy or of the labor.

In this paper we have not attempted to classify the underweight infants according to the method of delivery and have deferred comparison of the infants born by spontaneous delivery with those born after induction of labor.

Five infants who were born alive but died immediately after birth were not weighed; according to gestation periods, 1 was classified as full term and 4 were considered premature. Twenty-nine stillborn infants were not weighed; 8 of these were classified as full term and 21 as premature. There were also 25 abortions and 1 multiple abortion.

The present paper is limited to the consideration of the histories of the mothers of the 2,373 infants classified as single live births (column 1, table 1). The distribution of these infants according to sex and race is given in table 2. Further analyses of these factors will be elaborated in another report.

ANALYSIS OF INDIVIDUAL CAUSES OF PREMATURE DELIVERY

In table 3 is listed the frequency with which various conditions occurred in the mothers of underweight infants as compared with the incidence in the mothers of heavier infants. The data are arranged, for convenience, according to the birth weight of the child in ½ pound (227 Gm.) intervals, with summaries of the data relating to infants weighing less than 5 pounds (2,268 Gm.), to those weighing less than 5 pounds 8 ounces (2,495 Gm.) and, finally, to those weighing 5 pounds 8 ounces and more. The separate summaries of the data on the groups of premature infants weighing less than 5 pounds and less than 5 pounds 8 ounces were made to facilitate comparison with previous reports, which employed varying standards.

It appears that the incidence of some of these factors changes considerably with the inclusion, or the exclusion, of the mothers whose infants weighed at birth between 5 pounds and 5 pounds 8 ounces. More than one half of the infants weighing less than 5 pounds 8 ounces (108 of 206 infants) are within this limited weight range (chart).

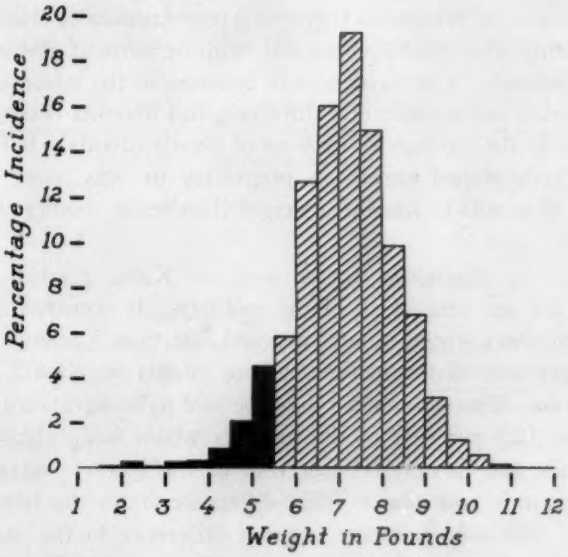
Toxemia.—This symptom occurred more frequently in the mothers whose infants weighed less than 5 pounds 8 ounces (25.7 per cent)

TABLE 3.—*Incidence of Various Conditions in Mothers of 2,373 Single Liveborn Infants*

Birth Weight of Infant	Number of Infants	Toxemia		Syphilis *		Serious Illness of Mother: Cardiac Disease		Serious Illness of Mother: Tuberculosis		Serious Illness of Mother: Other Conditions		Bleeding: Placenta Praevia		Bleeding: Premature Separation of Placenta		Bleeding: Unknown Cause		Abnormalities of Genital Tract: Pelvic Deformities		Abnormalities of Genital Tract: Myoma		Abnormalities of Genital Tract: Hydramnios		Trauma		No Known Abnormality	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
1 lb. to 1 lb. 7 oz...	1	..		..		..		1		..		..		..		..		..		..		..		..		..	
1 lb. 8 oz. to 1 lb. 15 oz...	2	..		..		..		..		1		..		1		..		..		..		..		..		..	
2 lb. to 2 lb. 7 oz...	7	..		..		..		..		1		..		..		3		..		..		1		2		..	
2 lb. 8 oz. to 2 lb. 15 oz...	2	..		..		..		..		1		..		1		1		..		..		..		..		..	
3 lb. to 3 lb. 7 oz...	7	2		3		1		..		..		..		1		2		..		..		..		1		1	
3 lb. 8 oz. to 3 lb. 15 oz...	9	3		..		..		..		2		..		..		3		..		..		..		..		2	
4 lb. to 4 lb. 7 oz...	21	9		4		..		..		..		..		1		5		2		1		..		2		1	
4 lb. 8 oz. to 4 lb. 15 oz...	49	11		5		..		..		4		..		2		12		..		1		..		1		11	
Total under 5 lb.....			25.5		12.5		1.0		1.0		9.2				6.1		26.5		2.0		2.0		1.0		6.1		15.3
5 lb. to 5 lb. 7 oz...	108	28		6		3		..		8		3		3		11		..		..		..		1		29	
Total under 5 lb. 8 oz..			25.7		8.9		1.9		0.5		8.3		1.5		4.4		18.0		1.0		1.0		0.5		3.4		21.4
5 lb. 8 oz. to 5 lb. 15 oz...	141	32		14		1		1		2		..		3		18		..		1		..		3		42	
6 lb. to 6 lb. 7 oz...	303	66		19		5		..		9		..		4		41		4		..		1		12		82	
6 lb. 8 oz. to 6 lb. 15 oz...	381	69		30		4		..		8		1		2		41		4		2		..		10		134	
7 lb. to 7 lb. 7 oz...	458	89		31		2		1		9		..		6		34		4		2		1		21		145	
7 lb. 8 oz. to 7 lb. 15 oz...	357	57		17		4		..		5		1		1		37		5		1		..		11		117	
8 lb. to 8 lb. 7 oz...	236	39		10		1		..		4		1		2		24		..		..		2		6		86	
8 lb. 8 oz. to 8 lb. 15 oz...	164	38		12		2		..		6		..		..		25		..		..		..		6		48	
9 lb. to 9 lb. 7 oz...	76	20		4		2		..		..		..		..		4		..		..		..		3		29	
9 lb. 8 oz. to 9 lb. 15 oz...	30	7		2		..		..		1		..		1		5		..		..		..		..		8	
10 lb. to 10 lb. 7 oz...	14	3		1		..		..		..		..		..		1		..		..		1		1		6	
10 lb. 8 oz. to 10 lb. 15 oz...	5	2		1		..		..		..		..		..		..		..		..		1		..		..	
11 lb. to 11 lb. 7 oz...	1	1		..		..		..		..		..		..		..		..		..		..		..		..	
11 lb. 8 oz. to 11 lb. 15 oz...	1	..		..		..		..		..		..		..		..		..		..		..		..		1	
Total 5 lb. 8 oz. and above			19.5		6.6		1.0		0.1		2.0		0.1		0.9		10.6		0.8		0.3		0.3		3.4		32.2
Grand total.....	2,373	476	20.0	159	6.8	25	1.1	3	0.1	61	2.6	6	0.3	28	1.2	267	11.3	19	0.8	8	0.3	7	0.3	80	3.4	742	31.3

* Serologic reports were not available for 24 mothers. The infants of 3 weighed less than 5 pounds 8 ounces (of whom 2 weighed less than 5 pounds), and those of the remaining 21 weighed 5 pounds 8 ounces or more.

than in those whose infants had a greater birth weight (19.5 per cent), a difference which is on the borderline of significance (table 4). Toxemia was about as frequent in the mothers whose infants weighed less than



Percentage distribution by weight of 2,373 single liveborn infants.

TABLE 4.—*Incidence of Toxemia in Mothers of 2,373 Infants*

	Toxemia	No Toxemia	Total
According to Race			
White	277	1,183	1,460
Negro	199	714	913
Total	476	1,897	2,373
($X^2 = 2.77$; P is between 0.10 and 0.05)			
According to Weight of Infant			
Less than 5 lb.	25	73	98
5 lb. and more	451	1,824	2,275
Total	476	1,897	2,373
($X^2 = 1.91$; P is between 0.20 and 0.10)			
	Toxemia	No Toxemia	Total
Less than 5 lb. 8 oz.	53	153	206
5 lb. 8 oz. and more	423	1,744	2,167
Total	476	1,897	2,373
($X^2 = 4.52$; P is between 0.05 and 0.02)			

5 pounds as in those whose infants weighed less than 5 pounds 8 ounces. Our figures for the incidence of this condition correspond closely with those reported by several other authors, but our conclusion is that

almost as many mothers of mature infants suffer from toxic manifestations as mothers of underweight infants. The wide variations of the incidence of toxemia, as reported, may be due to the different concepts of toxemia. We have included in the present category of toxemia those patients who had any symptoms suggesting preeclampsia or eclampsia and also the patients who had hypertension, with or without albuminuria at the time of delivery. The incidences of toxemia in the white and in the Negro race were not significantly different, and toxemia occurred about as frequently in the mothers of male as of female infants. It is possible that toxemia developed earlier in pregnancy or was more severe in the mothers of infants of low birth weight than in the mothers of heavier infants.

Syphilis.—As diagnosed by a positive Kahn reaction, syphilis occurred in 6.8 per cent of all of the mothers. It occurred in 8.9 per cent of the mothers whose infants weighed less than 5 pounds 8 ounces and in 6.6 per cent of the mothers whose infants weighed 5 pounds 8 ounces or more. This difference cannot be said to be significant. Syphilis was found in 12.5 per cent of the mothers whose infants weighed less than 5 pounds and in only 6.5 per cent of the mothers whose infants weighed 5 pounds and more. This difference is on the borderline of significance. There is, however, a great difference in the incidence of syphilis in the white and in the Negro mothers (table 5). A positive reaction to the Kahn test occurred in 11.3 per cent of the Negro mothers and in 3.9 per cent of the white mothers. This racial difference is of decided significance.

A positive reaction to the Kahn test occurred in 5.9 per cent of those white mothers whose infants weighed less than 5 pounds 8 ounces and in 3.8 per cent of those whose infants weighed more than that amount. This is not a significant difference. It occurred in 9.8 per cent of the white mothers whose infants weighed less than 5 pounds and in 3.7 per cent of those whose infants weighed more than that amount. This difference is on the borderline of significance.

In the Negro mothers there was no significant association of a positive reaction to the Kahn test with the production of an infant of low birth weight. A positive reaction occurred in 11.8 per cent of the mothers whose infants weighed less than 5 pounds 8 ounces and in 11.2 per cent of the mothers of the heavier infants. This is not a significant difference. A positive reaction occurred in 15.6 per cent of the mothers whose infants weighed less than 5 pounds and in 11.1 per cent of the mothers whose infants weighed 5 pounds and above. Apparently in this series if syphilis is associated with premature delivery, it is in the white rather than in the Negro patients and in the group producing infants of lower birth weight.

Other Illnesses of the Mother.—Cardiac disease, tuberculosis and other acute and chronic illnesses occurred so infrequently in our series that no analyses could be made.

Uterine Bleeding.—This symptom occurred more frequently among the mothers of infants with low birth weights than among those whose

TABLE 5.—*Incidence of Syphilis* in Mothers of 2,349 Infants*

According to Race

	Reaction to Kahn Test		
	Positive	Negative	Total
White	57	1,388	1,445
Negro	102	802	904
Total	159	2,190	2,349

($X^2 = 45.46$; P is less than 0.001.)

In White Mothers According to Weight of Infant

	Reaction to Kahn Test		
	Positive	Negative	Total
Less than 5 lb.	5	46	51
5 lb. and more	52	1,342	1,394
Total	57	1,388	1,445

($X^2 = 4.79$; P is between 0.05 and 0.02.)

	Reaction to Kahn Test		
	Positive	Negative	Total
Less than 5 lb. 8 oz.	6	95	101
5 lb. 8 oz. and more	51	1,293	1,344
Total	57	1,388	1,445

($X^2 = 1.14$; P is between 0.30 and 0.20.)

In Negro Mothers According to Weight of Infant

	Reaction to Kahn Test		
	Positive	Negative	Total
Less than 5 lb.	7	38	45
5 lb. and more	95	764	859
Total	102	802	904

($X^2 = 0.86$; P is between 0.50 and 0.30.)

	Reaction to Kahn Test		
	Positive	Negative	Total
Less than 5 lb. 8 oz.	12	90	102
5 lb. 8 oz. and more	90	712	802
Total	102	802	904

($X^2 = 0.03$; P is between 0.90 and 0.80.)

* Diagnosis of syphilis is based on a positive reaction to the Kahn test.

infants were heavier. Placenta praevia did not occur in any mother whose infant weighed less than 5 pounds, but it was diagnosed in 1.5 per cent of the women producing infants of less than 5 pounds 8 ounces and in 0.1 per cent of those giving birth to still heavier infants. The premature separation of a normally situated placenta or of a low implanted placenta occurred in 6.1 per cent of the mothers whose infants weighed under 5 pounds, in 4.4 per cent of those whose infants weighed

under 5 pounds 8 ounces and in 0.9 per cent of those whose infants weighed 5 pounds 8 ounces and above. Bleeding of other types occurred during the course of the pregnancy in 26.5 per cent of the women whose infants weighed under 5 pounds, in 18 per cent of those whose infants weighed under 5 pounds 8 ounces and in 10.6 per cent of those whose infants weighed 5 pounds 8 ounces and above. In this group we have included the women with symptoms of slight or occasional spotting or bleeding, a history of continued menses or bleeding which could not be attributed to placenta praevia or premature separation of a low or normally implanted placenta. When the incidence of this symptom in the mothers of infants weighing less than 5 pounds 8 ounces was

TABLE 6.—*Incidence of Bleeding of Unknown Cause in Mothers of 2,373 Infants*

	Bleeding	No Bleeding	Total
According to Race			
White	180	1,280	1,460
Negro	87	826	913
Total	267	2,106	2,373
($X^2 = 4.41$; P is between 0.05 and 0.02.)			
According to Weight of Infant			
Less than 5 lb.	26	72	98
5 lb. and more	241	2,034	2,275
Total	267	2,106	2,373
($X^2 = 23.90$; P is less than 0.001.)			
	Bleeding	No Bleeding	Total
Less than 5 lb. 8 oz.	37	169	206
5 lb. 8 oz. and more	230	1,937	2,167
Total	267	2,106	2,373
($X^2 = 10.17$; P is about 0.001.)			

compared with that in the mothers of infants weighing 5 pounds 8 ounces and more, the difference was statistically significant. The association of this symptom with low birth weight of the child was more marked when the group whose infants weighed less than 5 pounds was compared with the group whose infants weighed 5 pounds and more (table 6). The incidence of bleeding in the Negro women was 9.5 per cent, and in the white, 12.3 per cent. This difference is on the borderline of significance.

Local Abnormalities of the Genital Tract.—Pelvic deformities, myoma and hydramnios occurred too infrequently to evaluate.

Premature Rupture of the Membranes.—This accident appeared to be the cause of the premature delivery of 6.1 per cent of the infants weighing less than 5 pounds and of 2.9 per cent of those under 5 pounds 8 ounces. Causative factors for the premature rupture of the membranes could not be accurately determined, and satisfactory data could not be obtained from the control group.

TABLE 7.—*Age of Mothers of 2,373 Single Liveborn Infants*

Birth Weight of Infant	Age of Mother in Years														
	Under 15		15-19		20-24		25-29		30-34		35-39		40-45		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	Total
1 lb. to 1 lb. 7 oz.	..		1		..		..		..		..		..		1
1 lb. 8 oz. to 1 lb. 15 oz.	..		..		..		..		1		1		..		2
2 lb. to 2 lb. 7 oz.	..		2		3		1		1		..		..		7
2 lb. 8 oz. to 2 lb. 15 oz.	..		2		..		..		..		..		..		2
3 lb. to 3 lb. 7 oz.	..		3		3		..		1		..		..		7
3 lb. 8 oz. to 3 lb. 15 oz.	..		6		1		..		1		..		1		9
4 lb. to 4 lb. 7 oz.	..		7		6		3		4		1		..		21
4 lb. 8 oz. to 4 lb. 15 oz.	..		16		12		12		2		5		2		49
Total under 5 lb.	..			37.8		25.5		16.3		10.2		7.1		3.1	
5 lb. to 5 lb. 7 oz.	..		47		33		11		9		6		2		108
Total under 5 lb. 8 oz.	..			40.8		28.2		13.1		9.2		6.3		2.4	
5 lb. 8 oz. to 5 lb. 15 oz.	1		31		54		26		16		11		2		141
6 lb. to 6 lb. 7 oz.	2		87		119		58		22		13		2		303
6 lb. 8 oz. to 6 lb. 15 oz.	2		103		127		86		39		17		7		381
7 lb. to 7 lb. 7 oz.	5		115		163		104		42		21		8		458
7 lb. 8 oz. to 7 lb. 15 oz.	2		73		144		67		47		21		3		357
8 lb. to 8 lb. 7 oz.	..		40		83		50		37		20		6		236
8 lb. 8 oz. to 8 lb. 15 oz.	..		31		52		32		29		16		4		164
9 lb. to 9 lb. 7 oz.	..		11		24		18		14		5		4		76
9 lb. 8 oz. to 9 lb. 15 oz.	..		2		9		8		7		4		..		30
10 lb. to 10 lb. 7 oz.	..		1		5		5		1		2		..		14
10 lb. 8 oz. to 10 lb. 15 oz.	..		1		..		2		1		..		1		5
11 lb. to 11 lb. 7 oz.	..		..		..		..		1		..		..		1
11 lb. 8 oz. to 11 lb. 15 oz.	..		..		..		..		1		..		..		1
Total 5 lb. 8 oz. and above		0.6		22.8		36.0		21.0		11.9		6.0		1.7	
Grand total	12	0.5	579	24.4	838	35.3	483	20.4	276	11.6	143	6.0	42	1.8	2,373

TABLE 8.—*Gravidity of Mothers of 2,373 Single Liveborn Infants*

Birth Weight of Infant	Number of Children																				Total
	1		2		3		4		5		6		7		8		9		10 or More		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
1 lb. to 1 lb. 7 oz.	1		..		..		..		..		..		..		..		..		..		1
1 lb. 8 oz. to 1 lb. 15 oz.	..		..		..		..		..		1		..		..		..		1		2
2 lb. to 2 lb. 7 oz.	3		3		..		..		1		..		..		..		..		..		7
2 lb. 8 oz. to 2 lb. 15 oz.	2		..		..		..		..		..		..		..		..		..		2
3 lb. to 3 lb. 7 oz.	3		3		..		..		..		..		..		1		..		..		7
3 lb. 8 oz. to 3 lb. 15 oz.	4		2		..		2		..		..		..		..		1		..		9
4 lb. to 4 lb. 7 oz.	10		4		2		1		1		1		1		..		1		..		21
4 lb. 8 oz. to 4 lb. 15 oz	16		8		7		5		3		2		2		1		1		4		49
Total under 5 lb.		39.8		20.4		9.2		8.2		5.1		4.1		3.1		2.0		2.1		5.1	
5 lb. to 5 lb. 7 oz.	53		19		17		6		4		4		..		..		2		3		108
Total under 5 lb. 8 oz.		44.7		18.9		12.6		6.8		4.4		3.9		1.5		1.0		2.4		3.9	
5 lb. 8 oz. to 5 lb. 15 oz.	40		24		27		18		13		6		1		6		1		5		141
6 lb. to 6 lb. 7 oz.	116		69		47		19		22		11		4		4		4		7		303
6 lb. 8 oz. to 6 lb. 15 oz.	134		71		66		44		20		12		11		6		10		7		381
7 lb. to 7 lb. 7 oz.	154		111		61		50		27		22		11		7		5		10		458
7 lb. 8 oz. to 7 lb. 15 oz.	103		85		53		32		33		14		4		17		7		9		357
8 lb. to 8 lb. 7 oz.	47		58		45		24		13		13		11		8		6		11		236
8 lb. 8 oz. to 8 lb. 15 oz.	36		37		20		21		14		9		8		5		3		11		164
9 lb. to 9 lb. 7 oz.	11		13		17		11		3		8		7		..		3		3		76
9 lb. 8 oz. to 9 lb. 15 oz.	1		6		4		6		2		4		1		3		..		3		30
10 lb. to 10 lb. 7 oz.	1		5		2		3		1		1		..		..		..		1		14
10 lb. 8 oz. to 10 lb. 15 oz.	1		1		..		..		1		..		1		..		..		1		5
11 lb. to 11 lb. 7 oz.	..		1		..		..		..		..		..		..		..		..		1
11 lb. 8 oz. to 11 lb. 15 oz.	..		..		1		..		..		..		..		..		..		..		1
Total 5 lb. 8 oz. and above.		29.7		22.2		15.8		10.5		6.9		4.6		2.7		2.6		1.8		3.1	
Grand total	736	31.0	520	21.9	369	15.5	242	10.2	158	6.7	108	4.6	62	2.6	58	2.4	44	1.9	76	3.2	2,373

Traumatic Maternal Injuries.—Of the mothers whose infants weighed under 5 pounds, 6.1 per cent stated that they had sustained an injury of apparent consequence during the course of the pregnancy. The incidence of trauma in the mothers whose infants weighed under 5 pounds 8 ounces and the incidence in those whose infants were above this weight did not differ. In this series of cases there was no instance in which premature delivery could be directly and unreservedly attributed to trauma alone.

Maternal Age.—Table 7 is a comparison of the ages of the mothers of the infants in the various weight groups. In accordance with the conclusions of previous authors, there appears to be a predominance of young women among the mothers of the smaller infants. The mean age of the mothers whose infants weighed less than 5 pounds 8 ounces is 23 years, as compared with 24.3 years for the mothers of heavier infants. This difference, although small, is statistically significant. These figures may be influenced by the high incidence (31 per cent) of primiparas in our series. We plan to analyze this material more thoroughly.

Order of Birth.—In table 8 the order of birth of the underweight infants is compared with that of the heavier infants. It has seemed more logical to consider the order of birth in terms of gravidity, which includes every pregnancy regardless of outcome, rather than in terms of parity, which takes into consideration only those children born alive. At first glance, it would appear that an undue proportion of underweight infants occupy the first birth rank. These figures agree with the conclusions of several previous investigators. When, however, complete histories of all of the children of a family are considered and the previous premature births are included, it is possible that our conclusions will differ.

Season of the Year.—The monthly incidence of the underweight infants in this small series was greatest in July and smallest in October. The experience of several more years must be added before it is known whether this was a chance occurrence. Other authors have stated that the hours of sunshine available to mothers during their pregnancies influence the termination of the pregnancy.

Nonobstetric Surgical Procedures.—There were no instances of nonobstetric surgical procedures immediately preceding delivery in our series. A few of the women had undergone surgical operations earlier in the course of their pregnancies, without ill effects.

Fetal Anomalies.—No fetal anomalies occurred in the group of infants observed which were regarded as the cause of premature delivery.

Habitual Premature Delivery.—Some authors have considered this factor in their studies. Of the mothers of the infants in this series weighing under 5 pounds 8 ounces, 14.1 per cent gave a history of one or more previous premature terminations of pregnancy.

TABLE 9.—*Weights of Mothers and Infants*

Birth Weight of Infant	Number of Infants	Weight of Mother * in Pounds											
		Under 100		100-125		126-150		151-175		176-200		Over 200	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
1 lb. to 1 lb. 7 oz.	1	..		1		..		..		..		..	
1 lb. 8 oz. to 1 lb. 15 oz.	1	..		..		..		..		1		..	
2 lb. to 2 lb. 7 oz.	7	..		6		1		..		..		..	
2 lb. 8 oz. to 2 lb. 15 oz.	2	1		1		..		..		..		..	
3 lb. to 3 lb. 7 oz.	6	1		4		..		..		..		1	
3 lb. 8 oz. to 3 lb. 15 oz.	8	..		5		..		2		1		..	
4 lb. to 4 lb. 7 oz.	17	2		10		3		2		..		..	
4 lb. 8 oz. to 4 lb. 15 oz.	43	6		25		10		1		1		..	
Total under 5 lb.			11.8		61.1		16.5		5.9		3.5		1.2
5 lb. to 5 lb. 7 oz.	95	13		58		21		2		..		1	
Total under 5 lb. 8 oz.			12.8		61.1		19.4		3.9		1.7		1.1
5 lb. 8 oz. to 5 lb. 15 oz.	128	20		69		33		5		1		..	
6 lb. to 6 lb. 7 oz.	263	27		162		57		11		4		2	
6 lb. 8 oz. to 6 lb. 15 oz.	340	20		206		86		23		3		2	
7 lb. to 7 lb. 7 oz.	412	33		226		115		27		9		2	
7 lb. 8 oz. to 7 lb. 15 oz.	322	17		162		98		30		11		4	
8 lb. to 8 lb. 7 oz.	217	9		110		66		22		7		2	
8 lb. 8 oz. to 8 lb. 15 oz.	152	1		68		51		18		10		4	
9 lb. to 9 lb. 7 oz.	70	2		22		28		12		5		1	
9 lb. 8 oz. to 9 lb. 15 oz.	28	1		11		10		2		2		2	
10 lb. to 10 lb. 7 oz.	13	..		1		7		3		2		..	
10 lb. 8 oz. to 10 lb. 15 oz.	4	..		1		2		..		1		..	
11 lb. to 11 lb. 7 oz.	1	..		..		1		..		..		..	
11 lb. 8 oz. to 11 lb. 15 oz.	1	..		..		1		..		..		..	
Total 5 lb. 8 oz. and above			6.7		53.2		28.4		7.9		2.8		1.0
Grand total	2,131	153	7.2	1,148	53.9	590	27.7	161	7.6	58	2.7	21	1.0

* The weights of 242 mothers were not known.

Maternal Nutrition, Fatigue and Other Factors.—Numerous investigators have expressed the opinion that certain factors in the maternal nutritional status must be considered as factors possibly predisposing to premature delivery. It seems difficult to evaluate such material because of its indefinite character. When the average, nongravid weight of the mother was used as a criterion of her nutritional status, we found a predominance of small women among those producing small infants (table 9). So many other factors enter into the problem of nutrition that we cannot attempt to draw any conclusions.

TABLE 10.—*Antepartum Care* *

Birth Weight of Infants	Number of Infants	Antepartum Care					
		Inadequate		Intermediate		Adequate	
		No.	%	No.	%	No.	%
1 lb. to 1 lb. 7 oz.	1	1		..		..	
1 lb. 8 oz. to 1 lb. 15 oz.	2	2		..		..	
2 lb. to 2 lb. 7 oz.	7	4		3		..	
2 lb. 8 oz. to 2 lb. 15 oz.	2	2		..		..	
3 lb. to 3 lb. 7 oz.	7	6		..		1	
3 lb. 8 oz. to 3 lb. 15 oz.	9	6		1		2	
4 lb. to 4 lb. 7 oz.	21	8		7		6	
4 lb. 8 oz. to 4 lb. 15 oz.	49	28		11		10	
Total under 5 lb.			58.2		22.4		19.4
5 lb. to 5 lb. 7 oz.	108	50		27		31	
Total under 5 lb. 8 oz.			51.9		23.8		24.3
5 lb. 8 oz. to 5 lb. 15 oz.	141	60		36		45	
6 lb. to 6 lb. 7 oz.	298	113		98		87	
6 lb. 8 oz. to 6 lb. 15 oz.	380	163		116		101	
7 lb. to 7 lb. 7 oz.	456	179		130		147	
7 lb. 8 oz. to 7 lb. 15 oz.	354	124		105		125	
8 lb. to 8 lb. 7 oz.	233	83		77		73	
8 lb. 8 oz. to 8 lb. 15 oz.	164	67		51		46	
9 lb. to 9 lb. 7 oz.	76	24		25		27	
9 lb. 8 oz. to 9 lb. 15 oz.	30	4		13		13	
10 lb. to 10 lb. 7 oz.	14	7		3		4	
10 lb. 8 oz. to 10 lb. 15 oz.	5	2		2		1	
11 lb. to 11 lb. 7 oz.	1	..		..		1	
11 lb. 8 oz. to 11 lb. 15 oz.	1	..		..		1	
Total 5 lb. 8 oz. and above			38.4		30.5		31.2
Grand total	2,359	983	39.6	705	29.9	721	30.6

* Data on 11 patients whose histories are unknown and on 3 who were hospitalized are omitted from this table.

Twelve and six-tenths per cent of the women whose infants weighed under 5 pounds 8 ounces stated that they had not received sufficient rest during their pregnancies and that their duties had been out of proportion to their capabilities. The same history was obtained from only 6.4 per cent of the women giving birth to heavier infants. All of our patients came from the lower economic strata, but the majority of them had had no employment outside the home during the course of the pregnancy.

Illegitimacy.—A total of 9.7 per cent of the women producing underweight infants and 4.6 per cent of those producing heavier infants were unmarried. Illegitimacy was more frequent among the Negro patients.

Antepartum Care.—On the basis of the criterion of the Committee for the Evaluation of Prenatal Care [3] that six visits represent adequate care and three visits inadequate care, it appears that more of the women who produced premature infants were among those who did not have sufficient antepartum supervision. The available data are shown in table 10.

Unexplained Premature Delivery.—In our series 15.3 per cent of the mothers who gave birth to infants weighing less than 5 pounds, 21.4 per cent of those whose infants weighed less than 5 pounds 8 ounces and 32.3 per cent of those whose infants weighed 5 pounds 8 ounces and above had had no toxic manifestations, no complications of pregnancy, no infection or chronic disorder, no trauma and no bleeding during the antepartum period. Their reactions to the Kahn test were negative. Their pelvic measurements were within normal limits. A spontaneous or low forceps delivery of a vertex or breech presentation had followed the spontaneous onset of an uncomplicated labor.

SUMMARY AND CONCLUSIONS

We have presented a preliminary report of conditions in the mothers of 2,373 single liveborn white and Negro infants. We have considered, in the various birth weight groups, the frequency of the occurrence of certain factors presumed to predispose to the delivery of underweight infants. In general, it may be said that a history of illness or abnormality of the mother was obtained with greater frequency from women who gave birth to infants of low birth weight and, conversely, that a history of normal pregnancy and spontaneous delivery was obtained with increased frequency from those who bore heavier infants.

Antepartum bleeding of various types appeared to be definitely associated with low birth weight. Infants of low birth weight were frequently first born and born of young mothers; but in order that these data may be correctly interpreted, the complete obstetric history of the mothers must be considered and corrections made for size of family and for race. Illegitimacy was more frequent in the group of infants of low birth weight, but again allowance must be made for race, for gravidity and for other factors. While toxic manifestations occurred more frequently in the mothers of the infants of low birth weight, the association was not significant in this series. Syphilis occurred more often

3. Tyler, M.; Watkins, J. H., and Walker, H. H.: Report on the Evaluation of Prenatal Care, New Haven, Conn., The Institute of Human Relations, Yale University, 1934, p. 24.

in the Negro patients but was significantly associated with low birth weight only in the white mothers who produced infants with lower birth weights.

In this paper we have dealt only with the incidence of abnormal maternal conditions according to the birth weight of the infant. The study is being continued; and as the number of cases increases, it will be possible to study overlapping conditions and to investigate more closely certain factors which have been rather loosely grouped in this preliminary report. We believe that any definition of prematurity must take into account the race and the sex of the infant and perhaps also the age and the gravidity of the mother.

The Department of Obstetrics of the University of Cincinnati College of Medicine permitted us access to their patients and their records for this study.

Dr. Carl R. Doering and Mrs. James Bannon, of the Department of Vital Statistics of the Harvard School of Public Health, assisted in preparing the code which was used in the analysis of the data.

INTRADERMAL IMMUNIZATION

I. SCARLET FEVER

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Numerous investigations [1] have shown that active immunization is of value in preventing clinical scarlet fever. However, it is true that scarlatina sine eruptione may occur. Despite the possibility of successful immunization and the fact that, as is recognized, scarlet fever has been a mild disease in late years, it still carries an average annual death rate of 3.5 per hundred thousand population in Illinois [2] and frequently, even in the mild form, has serious complications and sequelae.

Hoyne stated [3] that routine immunization against scarlet fever has not been employed by some men, however, because of the severity of local and systemic reactions and because of the multiplicity of injections required. As a result, many modifications have been suggested to overcome some of these disadvantages of the Dick method. Thus, attempts have been made to immunize against scarlet fever by the oral administration of the toxin [4] and by administering the toxin intranasally [5] and by inunction.[6] Attempts have also been made, with some success, to prepare a scarlatinal streptococcus toxoid with formaldehyde which can be used as an antigen in producing immunity to scarlet fever.[7]

From the Children's Hospital, Illinois Soldiers' and Sailors' Children's School.

1. Dick, G. F., and Dick, G. H.: Scarlet Fever, Chicago, The Year Book Publishers, Inc., 1938, pp. 94-102 and 134-137.

2. Scarlet Fever, Educational Health Circular 59, Illinois Department of Public Health, June 1939, p. 13.

3. Hoyne, A. L.: Immunologic Methods in Pediatrics, J. A. M. A. **112**:1581 (April 22) 1939.

4. Cooke, J. V.: Entoral Administration of Scarlatinal Filtrate Toxin, Am. J. Dis. Child. **45**:54 (Jan.) 1933. Dick and Dick.[1]

5. Friedman, E.; Esserman, A. L., and Block, M. H.: Active Immunization Against Scarlet Fever by the Nasal Route, J. Pediat. **5**:504 (Oct.) 1934.

6. Martmer, E. E.: Immunization to Scarlet Fever by the Inunction Method, J. Pediat. **1**:555 (Nov.) 1932. Ripps, M. L.: Scarlet Fever Immunization by Inunction, ibid. **7**:754 (Dec.) 1935.

7. Veldee, M. V.: Preparation of a Scarlet Fever Streptococcus Toxoid and Its Use in Active Immunization, Pub. Health Rep. **48**:549 (May 26) 1933. Anderson, G. W.: Scarlet Fever Immunization with Formalinized Toxin: A Preliminary Report, Am. J. Pub. Health **28**:123 (Feb.) 1938.

It has long been recognized that the skin is an important organ concerned in the process of immunity and that it possesses the ability to form and store specific antibodies. As a result of this knowledge, immunization by the intradermal method has been attempted more extensively in recent years. Tuft,[8] in 1931, showed that the antibody response to typhoid vaccine injected intradermally was equal to that evoked by the subcutaneous method when only one-seventh the subcutaneous dose was used. Hence, he advocated the use of intradermal immunization against typhoid [9] because of its ease of administration and low percentage of constitutional reactions. Since this work, various reports have been made on immunization against scarlet fever by the intradermal method. Robinson [10] was able to render the Dick reactions of 24 subjects negative by the use of intradermal injections of one-twelfth the amount of the standard doses. Kern and associates [11] obtained a reversal of the Dick reaction in 90 per cent of subjects by the injection intradermally of amounts varying from 25 to 4,500 skin test doses. The number of injections ranged from three to ten; nevertheless, the duration of immunity was only six months in 60 per cent of subjects. Earle [12] produced immunity, as shown by negative Dick reactions, in 87 per cent of his subjects by use of three intradermal injections of as much as 1,600, 4,000 and 8,000 skin test doses, respectively. He reported that there were practically no local or systemic reactions.

For several years routine immunization against scarlet fever has been employed at the Illinois Soldiers' and Sailors' Children's School, and, as a result, the disease has been eliminated from the population.[13] However, we realize that the severity of the constitutional reactions may occasionally be serious enough to warrant not immunizing. One of us has seen a patient in whom acute toxic nephritis developed after immunization against scarlet fever.

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8. Tuft, L.: The Skin as an Immunological Organ, J. Immunol. **21**:85 (Jan.) 1931.

9. Tuft, L.: Active Immunization Against Typhoid Fever, with Particular Reference to an Intradermal Method, J. Lab. & Clin. Med. **16**:552 (March) 1931.

10. Robinson, J. H.: Active Immunization to Scarlet Fever by the Intracutaneous Method, J. Immunol. **31**:373 (Nov.) 1936.

11. Kern, R. A.; Crump, J.; Roddy, R. L., and Borow, S.: Scarlet Fever Immunization by the Intracutaneous Injection of Scarlatinal Streptococcus Toxin, J. Allergy **9**:125 (Jan.) 1938.

12. Earle, C.: Intradermic Immunization Against Scarlet Fever, Illinois M. J. **74**:248 (Sept.) 1938.

13. Peairs, R. P.: Immunization Against Scarlet Fever, Illinois M. J. **62**:246 (Sept.) 1932. Footnote 2.

REPORT OF A CASE

D. B., aged 6 years, entered the Milwaukee County Hospital Dispensary-Emergency Unit at 9 p. m. on Nov. 11, 1938. Forty-eight hours previously he had received a Dick test, to which he reacted positively, and on the following day he had received the first immunizing dose, of 500 skin test doses, by subcutaneous injection at one of the city clinics. One-half hour after the injection the patient began to vomit and to complain of abdominal pain. Diarrhea developed shortly, and the patient refused to take anything by mouth. These complaints continued until the time of entrance to the hospital.

The developmental and family histories were entirely normal. Birth was normal, but the patient had had infantile eczema until the age of 6 months, and, in addition, bronchopneumonia at 6 months, bronchitis at 1 year, two attacks of tonsillitis, pertussis at 5 years and measles one month prior to his entrance into the hospital.

The physical examination on entrance revealed a well developed, undernourished white boy who was stuporous and obviously dehydrated. The skin was dry and the tongue coated. The throat was not injected, and no rash was visible. The temperature on admission was 103.8 F.; the pulse, which was very faint, had a rate of 160 per minute, and the respiratory rate was 32. The blood pressure was 60 systolic and 52 diastolic, and the white cell count was 33,000 per cubic millimeter.

On November 12 the patient had signs of severe acidosis, with marked dehydration. Air hunger (typical Kussmaul respiration) and softness of the eyeballs were noted. A scarlatiniform rash appeared over the body, which persisted for three days. At this time the blood picture showed: white cells 46,500 and red cells 6,520,000, per cubic millimeter; hemoglobin content 16.5 Gm. per hundred cubic centimeters (107 per cent), polymorphonuclears (with toxic granules) 90 per cent, and large lymphocytes 5 per cent, small lymphocytes 2 per cent and monocytes 3 per cent. Marked azotemia was present, with the nonprotein nitrogen content of the blood 166.6 mg. per hundred cubic centimeters and creatinine 4 mg. The carbon dioxide–combining power of the blood (Van Slyke method) was reduced to 18.3 volumes per cent. Urinalysis showed a trace of bile and a 1 plus reaction for albumin, with 10 to 15 red blood cells per high power field and some coarse granular casts. The stools were green; no ova or parasites were noted, but many red and white blood cells were present. A culture of material taken from the throat on November 13 was negative for hemolytic streptococci and Klebs-Löffler bacilli.

Because of the marked acidosis and persistent vomiting, fluids were administered parenterally. On the third hospital day the temperature had dropped to normal and the vomiting and diarrhea subsided. The rash began to fade, and the tongue showed a typical strawberry marking. On November 15 results of chemical analysis of the blood were within normal limits, but the urine showed a 1 plus reaction for albumin and occasional erythrocytes.

The hemogram was normal on November 16. The sedimentation rate of the red blood corpuscles at this time was 81.75 per cent. The rash had cleared, and the patient was discharged to return home, under the care of a private physician. In view of the history and laboratory data, a diagnosis of acute toxic nephritis due to an injection of scarlatinal streptococcus toxin was made at that time.

PRESENT INVESTIGATION

This investigation was begun for the purpose of determining the proper dosage for intradermal injection in order to produce a high

percentage of negative Dick reactions, with a reduction in the number of injections and in the severity of constitutional reactions.

Material and Methods.—The Dick test was given to 1,120 children, ranging in age from 1.5 to 19 years, and positive reactions were obtained in 139 of them. One hundred and twenty of the children with positive Dick reactions were then given intradermal injections of scarlatinal streptococcus toxin. The subjects, selected at random sampling, were inmates of the Illinois Soldiers' and Sailors' Children's School at Normal, Ill., and the Lincoln State School and Colony at Lincoln, Ill. Since the latter institution is a school for mentally defective children, there is a high incidence of defects, so that the physical condition of these children is not on a par with that of the general population. However, none was excluded from the group because of his physical condition.

Institutional records of all subjects were examined for evidence of allergy. Urinalysis was done before and after immunization in the cases of all the children who received intradermal injections. We made careful observations, so that all systemic reactions, even of a mild nature, were recorded; all local reactions were measured. All children were given another Dick test two weeks after completion of the immunization and at varying intervals thereafter. Retests were all done on the forearm but at different locations in order to prevent the reading of reactions rendered falsely negative by the local antitoxic immunity produced by previous Dick tests.[14] Prior to immunization, 82 of the subjects were given control tests with Dick test material heated for one and a half hours in boiling water. The toxin used for immunizing was obtained on the open market from three different pharmaceutic houses.

The tests were done in accordance with the criteria laid down by the Dicks. Dry, autoclaved syringes were used, with acetone to cleanse the skin. The presence of the faintest erythematous patch 10 mm. in diameter after eighteen to twenty-four hours was regarded as a positive reaction.

On the basis of Earle's report,[12] it was decided to divide the children with positive Dick reaction into two groups. Group A received intradermally injections of 1,600, 3,200 and 8,000 skin test doses, respectively, of scarlatinal streptococcus toxin. Group B received three intradermal injections of 800, 1,600 and 3,200 skin test doses, respectively. The regular fifth dose of toxin for subcutaneous immunizing was so diluted with physiologic solution of sodium chloride that 0.1 cc. of solution contained the number of skin test doses necessary for each injection. These dilutions were made up fresh at the time of administration. The injections were all placed on the outer aspect of the upper part of the arm. It was found that the skin over the forearm was so tense that the local reaction from an injection caused considerable pain.

There were 29 subjects from the Normal school and 31 from the Lincoln school in each group. The 58 subjects at the Normal school received the injections at intervals of one week, while the 62 children at the Lincoln school received the second and third doses at two and four week intervals, respectively.

Results.—Group A.—Among the 60 children who received 1,600, 3,200 and 8,000 skin test doses of the toxin, constitutional reactions were encountered, although they were no more severe or frequent than

14. Dick, G. F., and Dick, G. H.: Local Immunity to Scarlet Fever, J. Infect. Dis. **62**:83 (Jan.) 1938.

those ordinarily seen with the subcutaneous method. Most of the reactions followed administration of the first dose. Those children who had the more severe reactions to the initial dose frequently had reactions to the second and third doses also. As a reaction to the injections (one hundred and eighty) given to this group, fever (temperatures ranging from 99 to 103 F.) developed twenty-one times (after 11 per cent of the injections), vomiting occurred eighteen times (after 10 per cent), headache developed thirteen times (after 7 per cent), and a scarlatiniform rash appeared three times (after 1.7 per cent). Altogether, 29 of the 60 children had some constitutional complaint following at least one injection. However, none of the reactions was alarming, and most of them were minor. Results of all urinalyses were negative after immunization.

In 1 girl, aged 11, a typical scarlatiniform rash developed twenty-four hours after the first injection, of 1,600 skin test doses. The tongue displayed the typical raspberry appearance. Pastia's lines were visible. A blanched area was present at the site of a former Dick test. Cultures of material taken from the nose and throat were negative for hemolytic streptococci. The eruption lasted for three days, and after a week desquamation, which was confined to the hands and feet, took place. One and one-half months later the Dick reaction was still positive, while the reaction to the control test was negative. Emesis occurred after a second injection of 1,600 units, and the reaction to the control test became strongly positive. A third dose, of 2,200 units, produced no reaction. Three months after the last dose reactions to both the Dick and the control test were negative.

The average local reaction to immunizing doses in this group measured 44.2 mm. in diameter. No abscesses were seen at the site of injection, and no tenderness in the regional glands occurred.

Of the 31 children in this group from the Lincoln school all had negative Dick reactions two weeks after the last injection. Three months later, 30 had negative Dick reactions; 1 child had died in the interim; therefore the reversal of the reactions remained 100 per cent.

Of the 29 children in this group from the Normal school, 25 (86.3 per cent) had negative Dick reactions one month after the third injection. Two of the 4 subjects with positive Dick reactions, however, also had positive reactions to the control material. Two months later 17 (58 per cent) of the 29 children showed negative Dick reactions, while 12 (41 per cent) showed equivalent erythematous reactions to the control and to the Dick test material. A retest one month later, or four months after the third injection, showed that 10 of the 12 had persistent positive reactions to the control test. However, the diameter of the cutaneous reactions was reduced in all cases, which would seem to indicate that sensitivity to the protein was not as marked. Six months after immunization 4 children still had positive reactions to the control test material. However, results of all Dick tests were read as

negative, since those children who showed erythematous reactions to the Dick test toxin had identical reactions to the control test material.

GROUP B.—Systemic reactions were also encountered in the 60 children who received 800, 1,600 and 3,200 skin test doses of toxin, respectively. However, almost all reactions were minor and occurred only about half as frequently as those seen in group A (see table 1). Again, the highest percentage of reactions followed the first dose of toxin. From the one hundred and eighty injections given, headache was complained of eleven times (after 6 per cent of the injections), fever (temperatures between 99 and 102 F.) appeared nine times (after 5 per cent) and emesis occurred nine times (after 5 per cent). A scarlatiniform rash was seen three times (after 1.7 per cent of the injections), but in no instance persisted for over twenty-four hours. Thirteen of the 60 children had some constitutional complaint from at least one injection, although in only

TABLE 1.—*Comparison of Systemic Reactions in Groups A and B*

	Group A (60 Subjects)		Group B (60 Subjects)	
	Number	Percentage	Number	Percentage
Symptoms following individual injections (180 in each group)				
Fever	21	11	9	5
Vomiting	18	10	9	5
Headache	13	7	11	6
Scarlatiniform rash	3	1.7	3	1.7
Total number of subjects with				
Some systemic complaint	29	48	13	21.6
Severe systemic reaction	2	3.3	0	0
Moderately severe systemic reaction	7	11.6	3	5

3 cases could the disturbance be classed as moderately severe. Again, results of all examinations of urine after immunization were negative.

In S. R., a boy aged 10 years, an anaphylactic-like reaction developed after the second and third doses of toxin, similar to the anaphylactic reactions to scarlet fever toxoid described by Wang.[15] Forty-five minutes after the second injection, of 1,600 skin test doses, he began to complain of weakness and generalized itching. Edema occurred about the eyes, the conjunctivas became congested and large wheals appeared over the body. A large wheal was also present at the site of injection (fig. 1). These complaints were quickly relieved by 7.5 minims (0.46 cc.) of epinephrine hydrochloride. Ten minutes after the third dose, of 3,200 units, similar symptoms developed, which were also relieved by epinephrine. The Dick test six months after the last dose caused erythema with wheal formation, but the control material elicited an identical reaction. The toxin was administered at one week intervals. No allergic history was elicited from the patient, but he had received one injection of diphtheria toxin-antitoxin nine years previously.

15. Wang, K. C.: Anaphylactic Reactions During Dick Test and Active Immunization with Scarlet Fever Toxoid, Chinese M. J. **53**:559 (June) 1938.

The local reactions in this group averaged 36.9 mm. in diameter. No local complications were observed.

One hundred per cent of the 31 children from the Lincoln school had negative reactions to the Dick test two weeks after the last injection. One child reacted positively, but the result of the control test was also positive. The results of a retest three months later showed that all 31 had negative reactions to the Dick test. Of the 29 children from the Normal school, 6 showed erythematous reactions to the Dick test toxin one month after the third dose. Of these 6 children, 3 also showed similar reactions to the control test material. Two months later there were 15 children (52 per cent) with positive Dick reactions, but all 15 had identical reactions to the control test. Four months after

Fig. 1.—S. R., showing wheal at site of injection and giant urticaria over trunk, which occurred ten minutes after injection of third dose, of 3,200 skin test doses intradermally, of scarlatinal streptococcus toxin.

the last dose 9 (31 per cent) still had positive reactions, but 8 continued to have positive reactions to the control test also. The 1 child whose reaction to the Dick test was positive and that to the control test negative was given a fourth dose, of 3,200 skin test doses, five months after the third dose. A Dick and a control test done on the same day resulted in reactions which were equal to the local reaction from the 3,200 units. Apparently, the toxin had stimulated the tissues, so that a state of hypersensitivity to the protein in the toxin was reestablished temporarily, for one month later the reaction to the Dick test was negative. Six months after immunization retests showed that all the children had negative reactions to the Dick test, although 2 continued to have positive reactions to the control test.

COMMENT

We believe that the intradermal method of immunization is superior to the subcutaneous method because of the decrease in severity of subsequent reactions resulting from the use of smaller doses and from the slower absorption of the toxin into the body. Furthermore, we believe that injection into the skin results in a higher antibody response, as shown by the reaction to the Dick test toxin, which is the only practical method available to measure immunity to scarlatinal streptococcus toxin. At the present time, we are employing the intradermal method for immunization against diphtheria at the Illinois Soldiers' and Sailors' Children's School with considerable success and for comparison are running series of subcutaneous and of intradermal immunizations against typhoid.

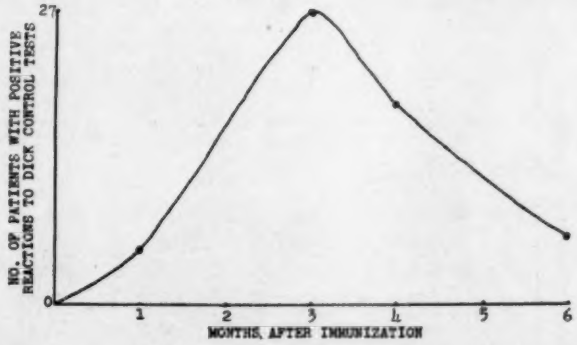

Fig. 2.—Frequency of hypersensitivity to protein of scarlatinal streptococcus toxin among 58 children at the Normal school.

Contrary to most reports, no relation was observed between the severity of the reactions and the age of the subjects, since reactions in the older children were not more severe. No relation was observed between the reactions and the allergic histories, but the number of subjects with allergic manifestations was not large, so that no statistical significance can be attached to this observation. It is interesting to note that no complaint of sore throat or joint pain was made after an immunizing dose by any of the children.

We found a considerable number of children with positive reactions to the control test after immunization and therefore feel justified in doing control tests on all children who react positively to the Dick test. Of the 58 children from the Normal school whom we had the opportunity to follow closely, we found 27 (46 per cent) who had positive reactions to the control test at some time after immunization. Sensitivity to the protein in the toxin reached its height about three months after the last dose of toxin (fig. 2). We attempted to determine if some other factor

was involved in producing this high percentage of positive reactions to the control test. The only other protein which these children received during the period of observation, however, was that contained in tuberculin test material (old tuberculin). No correlation could be found between the amount of tuberculin administered and the reaction to control and Dick tests; so we do not believe that there is a relation between the tuberculin protein and the protein of the scarlatinal streptococcus toxin (fig. 3).

Out of the entire series of 62 subjects at the Lincoln school, only 1 (1.6 per cent) showed a positive reaction to the control test. Since living conditions and the technic of immunizations have been similar at both institutions and the children are of comparable age and sex, the high incidence of positive reactions to the control test at Normal may possibly be explained by the difference in the time intervals at

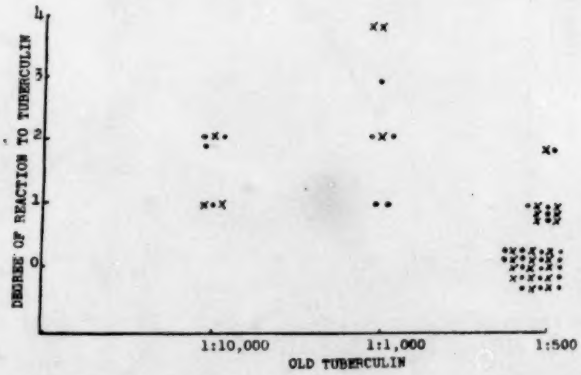

Fig. 3.—Relation between reactions to control Dick test and to tuberculin test in 58 children at the Normal school. In this chart, dots indicate a negative reaction, and crosses a positive reaction, to the control test.

which the toxin was administered or by the greater frequency of Dick retests given at this school.

In both group A and group B a reversal of the Dick reaction was obtained in 100 per cent of the subjects at the end of three months. A study of tables 2 and 3 shows that results of immunization obtained in the two groups are almost identical. However, giving the three doses of 800, 1,600 and 3,200 skin test doses (group B) is the more satisfactory method because of the reduction in the frequency and severity of reactions (see table 1).

As yet, we cannot say anything definite about the duration of immunity. Nevertheless, since the Dick reaction became negative in all subjects whereas with the subcutaneous method only 90 to 95 per cent of the

Dick reactions became negative,[1] it is reasonable to assume that the length of immunity will be at least as great as with the subcutaneous method.

During the period of observation a moderately severe epidemic of scarlet fever occurred in the county in which the school at Normal is located. Adult employees are not immunized, and as a result the school librarian had the disease. Despite her close contact with the children, no cases occurred in the student population.

TABLE 2.—*Results of Dick Retests After Immunization* at Lincoln State School and Colony*

	Group A (31 Subjects)		Group B (31 Subjects)	
	Number	Percentage	Number	Percentage
Two weeks after immunization				
Negative reaction to Dick test	31	100	31	100
Positive reaction to control test	0	0	1	3.2
Three months after immunization				
Negative reaction to Dick test	30	100	31	100
Positive reaction to control test	0	0	0	0

* Toxin was given at two and four week intervals.

TABLE 3.—*Results of Dick Retests After Immunization* at Illinois Soldiers' and Sailors' Children's School*

	Group A (29 Subjects)		Group B (29 Subjects)	
	Number	Percentage	Number	Percentage
One month after immunization				
Negative reaction to Dick test	27	93	26	90
Positive reaction to control test	2	7	3	10
Three months after immunization				
Negative reaction to Dick test	29	100	29	100
Positive reaction to control test	12	41	15	52
Four months after immunization				
Negative reaction to Dick test	29	100	28	96.5
Positive reaction to control test	10	34.4	8	27.6
Six months after immunization				
Negative reaction to Dick test	29	100	28	96.5
Positive reaction to control test	4	13.8	2	7

* Toxin given at one week intervals.

The intradermal method of immunization against scarlet fever possesses the distinct advantage over the subcutaneous method of reducing the number of injections from five to three. With the proper dosage, the reactions also are so reduced that one need not fear that the "reaction may be worse than the disease." Also, to institutions and health departments which do mass immunizations the cost of the toxin necessary for intradermal immunization can be reduced to one-eighteenth the cost by the subcutaneous method, because of the decreased amount of toxin required.

SUMMARY AND CONCLUSIONS

A case is presented of acute toxic nephritis due to subcutaneous injection of scarlatinal streptococcus toxin.

A 100 per cent reversal of the positive reactions to the Dick test was obtained in 120 subjects by the intradermal method of active immunization against scarlet fever.

The intradermal method of immunization against scarlet fever is superior to the subcutaneous method because of the fewer injections required and the decrease of subsequent reactions.

The optimal dose intradermally is 800, 1,600 and 3,200 skin test doses, administered on the outer aspect of the upper part of the arm at intervals of two and four weeks, respectively.

Epinephrine should be available whenever scarlatinal streptococcus toxin is administered so that anaphylactic reactions can be controlled.

Control tests should be done on all subjects with positive reactions to the Dick test.

Inoculation with tuberculin protein has no influence on the reaction to the protein of scarlatinal streptococcus toxin.

Dr. W. W. Fox, managing officer, and Dr. C. Katz, of the Lincoln State School and Colony, cooperated in providing case material for this study.

GUILLAIN-BARRÉ SYNDROME IN CHILDREN

A REVIEW OF THE LITERATURE AND REPORT OF THREE ADDITIONAL CASES

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In 1916, Guillain, Barré and Strohl described a syndrome in which there is slowly progressive ascending paralysis of the body, starting in the lower extremities, and which is characterized by albuminocytologic dissociation of the cerebrospinal fluid (increase in protein without an increase in the cell count) and a favorable prognosis. Previous to that time there were many reports of cases of polyneuritis resembling this syndrome, but they did not have detailed descriptions of the cerebrospinal fluid. Since then, there have been numerous cases reported of various neuritides which, although they do not have all the characteristics described by Guillain and his co-workers, nevertheless bear a resemblance to the syndrome and perhaps represent different degrees of severity of this disease of unknown cause.

Among these related syndromes, the following have been included: "acute infective polyneuritis," "acute febrile polyneuritis of unknown origin," "acute neuronitis," "acute benign infectious myelitis," "acute infective meningomyeloneuritis," "polyneuritis with facial diplegia," "myeloradiculitis," "infective neuronitis" and "radiculoneuritis."

The syndrome has the following history, symptoms and characteristics. The incidence is mainly in persons between the ages of 20 and 50 years, for the disease occurs only occasionally in the younger and older groups. The onset is usually slow, with a history of progressive paralysis, accompanied by paresthesias and muscular pain, affecting first the lower extremities and then the upper, with rare involvement of the respiratory muscles, though the muscles of the back and abdomen are frequently attacked. With the exception of the facial, the cranial nerves are rarely involved. The onset and course are usually afebrile, although fever or infection of the upper respiratory tract may precede the onset of paralysis. The paralysis, or paresis, is flaccid, with hypotonia but rarely with atrophy, the involvement being symmetric and more profound in the proximal than in the distal muscle groups. The deep reflexes

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are abolished or markedly diminished, and the superficial reflexes are usually present but may be absent. There are little change in the electrical reactions of the nerves or muscles and slight change in objective sensibility. Occasionally there are disturbances in sphincter control. The cerebrospinal fluid shows a constant and marked increase in protein, though it is usually not high early in the disease. There is no hypercytosis, and Guillain employed the term "albuminocytologic dissociation" to designate these findings. Xanthochromia may be present. The Wassermann reaction of the spinal fluid is negative. Slight precipitation may be present in the middle and end zones of the colloidal gold curve. The mental condition of the patient is unaltered. The prognosis is favorable, with recovery over a period of weeks or months, and there are usually no residual signs of the paralyses, although occasionally muscular atrophy, if present during the disease, persists. The deep reflexes may remain absent for weeks or months after recovery. Little pathologic material has been obtained, owing to the favorable outcome. In the cases that have been reported in which postmortem studies were made diffuse involvement was found, with the most marked changes in the spinal roots and peripheral nerves, less marked changes in the meninges and degenerative changes and hyperemia in the gray matter of the cord. The etiologic agent is still unknown; most authors favor the possibility of a virus or a toxic agent. There is no specific therapy. In the differential diagnosis, the main diseases to be considered are poliomyelitis, Landry's paralysis, the muscular atrophies and dystrophies and toxic neuritides, such as diphtheritic neuritis. In the disease last mentioned an albuminocytologic dissociation may be present.

The French prefer to designate the disease as the "Guillain-Barré syndrome." Guillain himself used the term "radiculoneuritis." Many American authors prefer the term "polyneuritis with facial diplegia" or "acute infective polyneuritis." Since the foregoing terms are descriptive of a syndrome rather than of a distinct disease entity and there are already too many confusing terms applied to the syndrome, and since Guillain and his co-workers were the first to point out the albuminocytologic dissociation and to stress the favorable prognosis, until the cause is discovered we favor the term "Guillain-Barré syndrome," although we are fully aware of the inadequacy of eponyms.

Although Guillain has stated that the disease is rare in children, in the past few years there has been reported an increasing number of cases occurring in younger persons. Three additional cases are here described, with the results of electroencephalographic examinations, which have not previously been reported, in 2 of them. We feel that it is important to stress the diagnosis of the condition, so that one not only may differ-

entiate it from such diseases as poliomyelitis, but, in view of the favorable outcome, may be able to give encouragement to the parents of the stricken child.

Table 1 is a résumé of the data in the cases reported in the English literature of the disease in children of 12 years or under. We realize that we may have overlooked some cases or that some may have been reported under a different designation.

Numerous discussions and case reports are found in the French literature. The entire issues of the *Journal belge de neurologie et de psychiatrie* for March and April 1938 are devoted to symposiums on the Guillain-Barré syndrome.

Nineteen cases of the syndrome in children of 12 years or under were found in the French literature. Of these, 9 were in children under the age of 5 years. Four cases occurred at 2 years, 2 at 3 years, 3 at 4 years, 2 at 5 years, 3 at 6 years, 1 at 7 years, 1 at 8 years, 2 at 10 years and 1 at 12 years of age. The sex distribution was about equal.

The following 3 cases occurred in patients at the Neurological Institute of New York.

REPORT OF CASES

CASE 1.—V. P., a white girl aged 12 years, entered the Neurological Institute as a private patient of Dr. A. Ferraro on April 29, 1937. Three weeks previously she had had an attack of tonsillitis, followed, a week later, by a sensation of pins and needles in the fingers and toes. On April 19 she had a feeling of "stiffness" in the legs, followed by progressive weakness of the extremities. On admission she had facial diplegia and weakness of all extremities. Deep and superficial reflexes were absent. There were no sensory disturbances, and the patient was mentally clear. The blood counts were essentially normal. The data from examination of the spinal fluid are presented in table 2. Cultures of material from the throat were sterile for Klebs-Löffler bacilli.

During her stay in the hospital the patient received physical therapy, massage and exposure to infra-red radiation. Vitamin B was given hypodermically. She was discharged on May 18, 1937, at which time there was little change in her condition.

Her progress was followed by Dr. Josephine Neal after her discharge from the hospital. Contractures had developed, but these gradually subsided in the next three months. Atrophy of all four extremities was present during the summer of 1937. Her muscular strength improved gradually during the fall and winter. By the spring of 1938 she had completely recovered and was riding horseback during the summer of 1938. There was a check-up of her condition in the spring of 1939, at which time she was apparently normal.

CASE 2.—W. P., a 2½ year old white boy, was admitted to the child neurology service on March 1, 1939. The past history was noncontributory. He had been well until January 17, six weeks previous to admission, when he fell off a chair, striking his back, without any apparent injury. He was able to rise and walk well. Three days later he complained of pain in the legs and thighs, which persisted, and he began to limp. On January 28 fever, cough and coryza developed, and his condition was diagnosed as "grip." The entire family was stricken with

TABLE 1.—*Summary of Data in Reported Cases of Guillain-Barré Syndrome in Children*

Source	Age, Yr.	Sex	Preceding Illness	Initial Symptoms and Date	Maximum Motor Involvement	Muscle Pain, Tenderness, Sensation	Reflexes	Spinal Fluid	Course and Comment
Thomson.....	5	M	Thrown out of boat 5 days before onset	Weakness of hands and feet, 1910	Paralyses of all extremities; facial diplegia	Numbness of fingers and soles	Not noted	No report	Recovery slow but complete in 2 years
Taylor and McDonald.....	7	F	Influenza 6 weeks previously, with recovery	Weakness and pain in legs, Jan. 27, 1919	Facial diplegia; arms and legs and muscles of neck and back weak	Pain in legs	Deep: absent	No report	Gradual improvement; well in September 1919
	7	M	Anorexia and irritability, March 27, 1931	Weakness of legs, unable to walk, March 28, 1931	Facial diplegia; generalized muscular weakness	Pains in thighs	Deep: absent; superficial: present	1 cell; 222 mg. of protein/100 cc.; slight xanthochromia	Died April 30, 1931, of virulent streptococcic infection of throat
Ford.....	3	M	Mild infection of upper respiratory tract for 2 days	Weakness of legs, 10 days later	Legs paralyzed; shoulder muscles weak	Loss of sensibility in lower half of back and shoulders	Deep: absent	3 cells; excess of protein	Improved 1 month after onset; well 1 year later; increased ankle and knee jerks
Hecht.....	10	F	Toothache, Dec. 18, 1927	Legs weak, Dec. 24, 1937	Weakness in all extremities, greater in legs	No pain	Deep: absent; superficial: present	1 cell; result of Pandy test +	Improved in few weeks; well on May 8, 1928
	10	F	Pain in knees, in spring 1930	Weakness of arms, September 1930; admitted Dec. 1, 1930	Facial diplegia; weakness in thighs, hips and arms	No pain	Deep: diminished	5 cells; result of Pandy test negative	Improved in February 1931
			Pneumonia; December 1931	Readmitted, December 1931	Generalized muscular weakness, as if dystrophic	.....	.....	.....	Second discharge in January 1932, improved; died August 1932, of "myocarditis"
	7	F	Bronchitis with fever Oct. 15, 1930; cold in head Oct. 30, 1930	Dragged legs; poor use of hands	Weakness in all extremities; unable to sit up	No pain	Deep: absent	2 cells; result of Pandy test ++	Improvement began Jan. 7, 1931; contractures of both achilles tendons
	2	F	Cold 12 days before admission	Weakness of legs, Nov. 2, 1934	Legs paralyzed; trunk, arms and neck muscles weak; difficulty in swallowing	Hypesthesia of lower extremities	Deep: absent	16 cells; reaction to Pandy test +	Slow improvement; fully recovered in November 1935
	3	F	None; injected throat on admission	Pain in arms and legs, Dec. 10, 1934	Helpless; unable to sit or hold head up	No pain	Deep: absent	9 cells; reaction to Pandy test ++++	Condition stationary for weeks; discharged as well July 25, 1935

	3	M	Cold 2 weeks before admission; fell down stairs Feb. 1, 1935. uninjured	Stumbled frequently, Feb. 5, 1935	Legs paralyzed; trunk and shoulder muscles weak	No pain	Deep: absent; superficial: present	3 cells; reaction to Pandy test +++	Improved November 1935; well in February 1936
	8	F	Collapsed Feb. 26, 1937, unable to stand	Admitted March 1, 1937	Generalized weakness	Muscle pain	Deep: absent; superficial: present	2 cells; reaction to Pandy test ++	Fully recovered, April 19, 1937
Mettel.....	5	M	Slight fever, sore throat	Weakness of legs few days later	Generalized weakness, including abdominal muscles; required artificial respiration for few hours; facial diplegia	Not noted	Deep, absent	Result of lumbar puncture reported as negative	Recovery completed after 5 weeks; reflexes normal
	11	F	Fell Sept. 1, 1922; soreness in knees and legs	Weakness of legs, Sept. 2, 1922; vomited frequently	Weakness of arms and legs	Pain in shoulders and hips	Deep: sluggish	11 cells; result of test for globulin +	No report on sequelae
Gilpin, Moersch, Kernohan	2	F	Cold in December 1933	Weakness in legs, December 1933	Arms and legs very weak	No pain	Deep: absent	1 cell; result of Pandy test ++	Gradual improvement
	6	F	Scarlet fever in February 1934	Weakness of legs, April 1934	Generalized weakness in June 1934	Pains in back	Deep: absent	1 cell; 200 mg. of protein/ 100 cc.	Complete recovery in 8 months
	4	M	Sore throat in February 1934	Weakness in legs, July 1, 1934	Facial weakness; arms and legs weak	No pain	Deep: absent	8 cells; 240 mg. of protein/ 100 cc.	Recovery in 5 months
	12	F	Fever in September 1934	Pains in legs, 1 week later	Weakness of legs	No pain	Deep: diminished	5 cells; 120 mg. of protein/ 100 cc.	Weakness still present October 1934
Bassoe.....	3	F	None; positive reaction to tuberculin test before admission	Dragged right foot, March 1936; tonsillitis on admission, April 9, 1936	Atrophy of leg muscles below knees	No pain	Absent on admission; varied at intervals; at times hyperactive	3 cells; 660-2,080 mg. of protein /100 cc.	Enlarged cervical glands, papilledema, fever on admission; discharged as well on Jan. 13, 1937, ankle clonus, Babinski sign but no papilledema
Gillespie and Field.....	6	M	Frequent gum boils, carious teeth, 6 months previously	Progressive paralyses, January 1938	Paralyses of all extremities; moderate atrophy of muscles	Muscle tenderness	Deep: absent; superficial: present	No cells; result of Pandy test ++++	Improved after tonsils, adenoids and carous teeth removed; 90% improved August 1938

similar symptoms at the same time. The patient recovered from the acute illness in four days, but when he attempted to get out of bed and stand, his feet gave way under him. The weakness of the legs continued, and four days before admission he complained of pains in the arms, and marked weakness of the upper extremities developed. His voice became weak. After the onset of his illness, he had occasional spells of vomiting, gagged at times when given food and took longer to swallow his food.

On admission he showed marked generalized muscular weakness and, except for his head, there were few spontaneous movements. Flaccid paralyses of all extremities were present, and he was unable to sit up without support. The deep and superficial reflexes were absent. Breathing was shallow, but there was no respiratory embarrassment. He perspired freely, especially on the head. Sensory examination was unsatisfactory.

TABLE 2.—*Data from Examination of Spinal Fluid* in Case 1*

Date	Cells	Globulin Reaction	Total Protein Mg./100 Cc.	Sugar, Mg./100 Cc.	Chlorides, Mg./100 Cc.	Colloidal Gold Curve
4/28/37	2	3+	250	74	...	1111122221
4/30/37	3	3+	248	120 †	730	1111122221
5/ 3/37	5	3+	250	78	725	
5/17/37	3	3+	300	82	730	

* The Wassermann reaction and the results of smears and cultures of the spinal fluid were negative.
† After intravenously administered dextrose.

TABLE 3.—*Data from Examination of Spinal Fluid* in Case 2*

Date	Cells	Globulin Reaction	Total Protein Mg./100 Cc.	Sugar, Mg./100 Cc.	Chlorides, Mg./100 Cc.	Colloidal Gold Curve
3/ 3/39	0	2+	126	..	747	1100000000
3/ 8/39	3	2+	130	77	729	
3/17/29	2	1+	83	69	731	
3/30/39	3	1+	77	66	...	
4/20/39	0	0	40	56	746	

* The Wassermann reaction and the results of smears and cultures of the spinal fluid were negative.

The roentgenogram of the skull was normal. Roentgen examination of the spine showed the spinous processes of the fifth lumbar vertebra to be poorly fused. The spinous processes of the two upper sacral vertebrae were not well fused, and the first sacral vertebra showed a tendency toward lumbarization. The roentgenogram of the chest was normal, with no evidence of tuberculosis.

Psychometric examination revealed an intelligence quotient of 129.

The results of blood counts and urinalysis were normal. Cultures of material from the nose and throat were negative for Klebs-Löffler bacilli. The reaction to the tuberculin test was positive. The results of the Kline test were negative. The data from examination of the spinal fluid are listed in table 3.

The results of the electroencephalographic examination performed on March 3 were reported as follows: Pathologic alterations consisted of bursts of slow waves, from 3 to 6 per second, appearing generally over both hemispheres, but

better defined posteriorly over the occipital lobes and parieto-occipital regions. Intermittent foci for these waves were established bilaterally over these regions. There was some indication of lateralization to the right of the area of slow activity in the postcentral region. The pathologic slow waves were suggestive of decelerated alpha waves. They were, for example, abolished by opening the eyes and in frequency shaded into the normal alpha rate, for the patient's age, of 7 to 8 per second.

In a later electroencephalogram, taken on March 26, certain changes were noted. The outstanding component again was a large smooth 5 to 6 per second wave. This wave now seemed to be more diffuse in its distribution, although it was still better defined posteriorly. The lateralization to the right over the postcentral region was still maintained, and, in addition, there was a recurrent lateralization to the left, over the precentral region, not noted in the earlier observations. The slow (2 to 3 per second) delta component also now appeared definitely less well defined than in the earlier observations. A new feature of the patterns was the large wave-spike contours which appeared intermittently in paroxysmal bursts against the 5 to 6 per second activity.

TABLE 4.—*Data from Examination of Spinal Fluid in Case 3*

Date	Cells	Total Protein, Mg./100 Cc.	Chlorides, Mg./100 Cc.	Sugar, M./100 Cc.
2/ 1/40	9	123	729	63
2/ 6/40	3	112		
2/15/40	3	92		
2/23/40	2	67		
3/ 1/40	8	56		
	(red cells 6,200; bloody tap)			
3/14/40	4	54		
	(red cells 115)			

The general impression was that of an abnormal electroencephalogram, with evidence of diffuse bilateral disturbance of normal cortical activity.

Course.—The patient had occasional rises in temperature to 101 F. during the first week, which were explained on the basis of mild coryza and the presence of enlarged, infected tonsils. After the first week he began to show progressive improvement in muscular strength. The improvement was in inverse order to the onset of the involvement of the muscle groups. By March 21 the strength of his arms was good, so that he was able to feed himself. By April 1 he was able to sit up without support. Two weeks later he was able to stand, and he was walking on April 18, though the gait was slightly wobbly. He was discharged on May 8. When he was seen in the clinic a month later, he was walking well. He had regained his muscular strength, but the deep reflexes did not return until about eight months after the onset.

CASE 3.—A. K., a white boy aged 3 years, was admitted to the Neurological Institute on Jan. 30, 1940. Five days previously he had had a sudden onset of symptoms, with unsteady gait and falling every few steps. There were no preceding illnesses. His condition became rapidlly worse, so that within three days he was unable to stand or walk. Pains and weakness of the arms developed on January 29. There were no febrile reactions; the only other symptom was that of restlessness. The past history was irrelevant.

Physical examination revealed a well developed, thin boy who was unable to raise himself to a sitting position or stand without support. Generalized hypotonia

was present. The deep reflexes were unobtainable in the lower extremities, except for the achilles reflex. In the upper extremities they were sluggish. The superficial reflexes were present. The Babinski sign was obtained bilaterally. Sensation was normal. There was questionable weakness of the lower half of the left side of the face. Results of the remainder of the examination were normal.

The results of blood counts and urinalysis were normal. The roentgenogram of the skull was reported to be normal. Psychometric examination revealed an intelligence quotient of 132. The result of the Kline test was negative. The data from examination of the spinal fluid are reported in table 4.

The following is a report of the reading of the electroencephalogram: Insufficient cooperation was obtained. The available records showed prevailing normal alpha rhythms, at 8 to 9 per second, over both sides, with intermixed random slow waves of a low amplitude, at 3 to 6 per second. No consistent bilateral difference or foci were observed, and the random slow activity was apparently within normal limits for a child of his age. The impression was that of an electroencephalogram within normal limits.

The patient received 2 mg. of thiamine hydrochloride (N. N. R.) three times daily. Diathermy over the spine, a procedure which had been found beneficial to an adult, was tried on the patient, but was discontinued when there were no striking effects over a period of one month.

Two weeks after admission the strength in the arms began to return and he was able to raise his arms above the shoulders. A week later he was able to raise his legs off the bed. His improvement was then gradual. By March 20 he was able to stand and take short steps. After this his gait improved steadily, and deep reflexes were now present. At the time of his discharge, on April 2, he was ambulatory but was still taking short steps.

SUMMARY

Radiculoneuritis of unknown causation, characterized by development of progressive flaccid paralyses in ascending order, with albuminocytologic dissociation in the spinal fluid and with good prognosis, is described under the name of the Guillain-Barré syndrome. Three additional cases of the disease in children are added to those already reported in the literature.

BIBLIOGRAPHY

Babonneix, L., and Lévy, M.: Syndrome de radiculo-névrite avec dissociation albumino-cytologique chez une petite fille de quatre ans, Gaz. d. hôp. **107**:117 (Jan. 24) 1934.

Bassoe, P.: Guillain-Barré Syndrome and Related Conditions, Arch. Path. **26**: 289 (July) 1938.

Bradford, J. P.; Bashford, E. F., and Wilson, J. A.: Acute Infective Polyneuritis, Quart. J. Med. **12**:88, 1918.

Casamajor, L.: Acute Ascending Paralysis Among Troops, Arch. Neurol. & Psychiat. **2**:605 (Dec.) 1919.

Clement, M., and Ketelbant: Syndrome de Guillain et Barré et varicelle chez un enfant, J. belge de neurol. et de psychiat. **38**:240 (March) 1938.

Cohen: À propos de trois enfants présentant certains caractères du syndrome de Guillain-Barré, J. belge de neurol. et de psychiat. **38**:307 (April) 1938.

Dagnelie, J.: Remarques sur quelques observations de polyradiculonévrites avec dissociation albumino-cytologique et à évolution favorable, J. belge de neurol. et de psychiat. **38**:282 (April) 1938.

Debré, R.; Marie, J., and Messimy: Polynévrite pseudo-myopathique, Bull. Soc. de pédiat. de Paris **32**:322 (June) 1934.

Ford, F.: Diseases of Nervous System in Infancy, Childhood and Adolescence, Springfield, Ill., Charles C. Thomas, Publisher, 1927, p. 553.

Gillespie, J. B., and Field, E. H.: Acute Polyneuritis of Uncertain Origin, J. Pediat. **14**:363 (March) 1939.

Gilpin, S. F.; Moersch, F. P., and Kernohan, J. W.: Polyneuritis, Arch. Neurol. & Psychiat. **35**:937 (May) 1936.

Giraud, P., and Boudouresques, J.: Radiculo-névrite avec dissociation albumino-cytologique du liquide céphalo-rachidien (syndrome de Guillain et Barré) chez infant. À propos de quatre observations personnelles, J. belge de neurol. et de psychiat. **38**:256 (April) 1938.

Guillain, G.: Radiculoneuritis with Acellular Hyperalbuminosis of the Cerebrospinal Fluid, Arch. Neurol. & Psychiat. **36**:975 (Nov.) 1936.

——Barré, J. A., and Strohl, A.: Sur un syndrome de radiculo-névrite avec hyperalbuminose du liquide céphalo-rachidien sans réaction cellulaire, Bull. et mém. Soc. méd. d. hôp. de Paris **40**:1462 (Oct. 13) 1916.

Hecht, M. S.: Acute Infective Polyneuritis, J. Pediat. **11**:743 (Dec.) 1937.

Mettel, H. B.: Acute Infective Polyneuritis in Children with Report of Cases, J. Michigan M. Soc. **23**:47-49 (Feb.) 1924.

Meyer, M. R.: À propos d'un nouveau cas de syndrome de Guillain et Barré chez un enfant, Rev. neurol. **2**:617 (Nov.) 1934.

Sands, I.: Acute Benign Infectious Myelitis, J. A. M. A. **96**:23 (Jan. 3) 1931.

Strauss, I., and Rabiner, A.: Myeloradiculitis: Clinical Syndrome with Report of Seven Cases, Arch. Neurol. & Psychiat. **23**:240 (Feb.) 1930.

Taylor, W. W., and McDonald, C. A.: The Syndrome of Polyneuritis with Facial Diplegia, Arch. Neurol. & Psychiat. **27**:79 (Jan.) 1932.

Thomson, F. G.: Acute Toxic Polyneuritis, Brit. M. J. **2**:1443, 1910.

Van Bogaert, L., and Maere, M.: Les polyradiculonévrites crâniennes bilatérales avec dissociation albumino-cytologique, J. belge de neurol. et de psychiat. **38**:275 (April) 1938.

——Phillips, F.; Radermecher, J.; Radermecher, M. A., and Verschraegen, T.: Essai sur un groupe épidémique de cas de poly-radiculonévrite avec dissociation albumino-cytologique du liquide céphalo-rachidien, ibid. **38**:151 (March) 1938.

Viets, H.: Polyneuritis with Facial Diplegia, Arch. Neurol. & Psychiat. **17**:794 (June) 1927.

NORMAL BLOOD SUGAR VALUES IN CHILDREN

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The work that led to the data in this paper was initiated by the paucity of published observations on blood sugar values in normal children of different ages. Frequently we have encountered in our juvenile patients with diabetes blood sugar levels that seemed much lower than normal, and indeed below what authorities commonly consider the lower limit of normal, but despite this the children have insisted that they felt quite well, that they were not weak and that they had no symptoms of insulin reaction, with which practically all our patients at some time have had experience. In attempting to correlate our reports on blood sugar levels with the symptoms or lack of symptoms in our patients, we have resorted to the literature repeatedly, without obtaining convincing data on normal blood sugar values in children between the ages of 2 and 16 years. Undoubtedly there have been many reports published in conjunction with other data, but in such an enormous volume of printed material as is indexed in the *Quarterly Cumulative Index Medicus* they have not found a place under subjects where references to blood sugar values were listed.

In order to obtain normal blood sugar values on children, we selected a group of nondiabetic children who were well nourished and afebrile and, as far as we could ascertain, had no history of diabetes among their relatives. From this group of children we collected specimens of venous blood, both during fasting and at 11 a. m., taking care particularly that the patients had eaten their breakfasts at least three and one-half hours before the second specimen was taken. Both specimens were collected the same day from all subjects included in this report. All the patients were in the James Whitcomb Riley Hospital for Children at the time the study was made; all were on adequate, well balanced diets and were afebrile.

This work was made possible by a grant from the Research Committee of the Indiana University School of Medicine.

From the departments of medicine and pediatrics of Indiana University School of Medicine, and the James Whitcomb Riley Hospital for Children.

Many of the children were under orthopedic care; part of them were convalescing from acute infectious states, but their infections were sufficiently remote that the results were not influenced by toxemia.

For many years we have found it convenient in the diabetic outpatient clinic to use blood sugar values determined on blood taken at 11 a. m., although many times we have been criticized for relying on such values rather than on fasting blood sugar levels in evaluating the patient's response to treatment. Furthermore, we have observed that we have received more help from blood sugar levels of specimens drawn before the noon meal when patients are on regular insulin therapy. Because of our experience with blood sugar values determined on specimens drawn at 11 a. m., both of the patients in the hospital and of those in the outpatient clinic, we were curious to learn the actual difference, if any, between fasting and 11 a. m. blood sugar levels. To correlate the observations the two specimens of blood from each child were drawn on the same day.

The Folin-Wu [1] method for the determination of the sugar was used. Somogyi and Ronzoni [2] emphasized the fact that there are reducing substances in the blood which alter blood sugar values when determinations are made by several well known methods. They also stated that the value for the "true sugar" is less than that commonly reported. Methods have been proposed which will give a more accurate reading of the "true sugar" value, but in formulating our plans for collecting these data we were influenced in selecting the Folin-Wu method because of its routine use in many hospital laboratories, including our own. As a clinical test it is dependable and relatively free from technical difficulties.

BLOOD SUGAR VALUES IN ADULTS

Information on normal blood sugar levels may be found in many textbooks and periodicals. Aside from the reports on blood sugar values in infants, the English and American literature contains little on blood sugar levels in normal children. Most reports refer to values for blood sugar in adults. For comparison, we have compiled table 1 from the data of various authors.

Cursory inspection of table 1 emphasizes the rather wide fluctuation of normal readings. It also reveals considerable variation in results with different methods of determination of the sugar. There is an interesting uniformity in those methods that give values between 70

1. Folin, O., and Wu, H.: A Simplified and Improved Method for Determination of Sugar, J. Biol. Chem. **41**:367 (March) 1920.

2. Somogyi, M., and Ronzoni, E.: The Presence of a Polysaccharide-Like Substance in Blood, Proc. Soc. Exper. Biol. & Med. **24**:220 (Dec.) 1926.

mg. per hundred cubic centimeters and 105 mg., which are more nearly the values for "true sugar," but on the whole the table indicates that values for about 90 per cent of the subjects fall between 70 mg. per hundred cubic centimeters and 120 mg. The values for 86.3 per cent of Gray's [3] 431 subjects and for 75.2 per cent of John's [4] 1,000 subjects varied from 70 to 110 mg. per hundred cubic centimeters.

TABLE 1.—*Values for Normal Fasting Blood Sugar in Adults.*

Author	Method	Blood Sugar Value, Mg. per 100 Cc.
Todd, J. C., and Sanford, A. H.: Clinical Diagnosis by Laboratory Methods, ed. 9, Philadelphia, W. B. Saunders Company, 1939	Not stated	90 to 120
Hawk, P. B., and Bergeim, O.: Practical Physiological Chemistry, ed. 11, Philadelphia, P. Blakiston's Son & Co., 1937	Several methods	70 to 120
	Folin-Wu	90 to 120
	Folin-Malmros micromethod	75 to 105
	Hagedorn-Jensen micromethod	75 to 105
	Folin's modification of Folin-Wu	75 to 105
	Benedict's copper reduction	70 to 100
	Somogyi-Shaffer-Hartman	70 to 100
Glassberg, B. Y.: Proc. Soc. Exper. Biol. & Med. **28**: 889 (June) 1931	Somogyi-Shaffer-Hartman	70 to 95
John [4]	Myer-Bailey (on 1,000 subjects)	60 to 160
	87.6 per cent of 1,000 subjects	70 to 120
	75.2 per cent of 1,000 subjects	70 to 110
Gray [3]	Not stated (data for 431 subjects collected from the literature)	40 to 160
	90.7 per cent of 431 subjects	70 to 120
	86.3 per cent of 431 subjects	70 to 110
Dionne, M. J., and Arenstam, J. J.: J. Biol. Chem. **87**: 393 (June) 1930	Folin-Malmros (subjects were all young women)	86 to 101
Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1931, vol. 1	Not stated	70 to 120
Joslin, E. P.: Treatment of Diabetes Mellitus, ed. 6, Philadelphia, Lea & Febiger, 1937	Not stated	70 to 120

BLOOD SUGAR VALUES IN INFANTS

In reviewing the literature on blood sugar levels in infants, we likewise found a great fluctuation in normal values. To illustrate this, we compiled table 2. From careful study of table 2 one gains the impression that the normal blood sugar level in infants usually is between 60 and 100 mg. per hundred cubic centimeters. There are a few values as low

3. Gray, H.: Blood Sugar Standards: Normal and Diabetic Persons, Arch. Int. Med. **31**:241 (Feb.) 1923.

4. John, H. J.: A Study of Fasting Blood Sugar and Urea in Nondiabetic Patients, Ann. Clin. Med. **5**:340 (Oct.) 1926.

as 50 mg. per hundred cubic centimeters and some as high as 110 mg., but these are exceptions, similar to those reported to occur in adults both by John and by Gray.

Tisdall, Drake and Brown [5] summarized average values for fasting blood sugar in infants, obtained by the Bang method, and concluded that most series of averages published on infants ranged between 75 and 90 mg. per hundred cubic centimeters. They reported values for 68 patients of their own, determined by the Shaffer-Hartman method, which had an average of 85 mg. per hundred cubic centimeters and a range from 58 to 109 mg. per hundred cubic centimeters. Sedgwick and Ziegler's [6] average value for newborn infants was 82 mg. per hundred cubic centimeters, with limits of variation from 50 to 110 mg. per hundred cubic centimeters.

TABLE 2.—*Values for Normal Fasting Blood Sugar in Infants*

Author	Age of Subject	Method	No. of Subjects	Blood Sugar Value, Mg. per 100 Cc.
Sedgwick and Ziegler [6]	3 to 43 days	Folin-Wu	46	50 to 110
Tisdall, Drake and Brown [5]	1 to 18 mo.	Shaffer-Hartmann	68	58 to 109
Guy, R. A.: Quart. J. Med. **15**: 9 (Oct.) 1921	Infants	Lewis-Benedict	11	60 to 90
Greenwald, H. M., and Pennell, S.: Am. J. Dis. Child. **39**: 281 (Feb.) 1930	Up to 13 days	Folin micromethod	94	60 to 100
Brown, M. J.: Quart. J. Med. **18**: 175 (Jan.) 1925	Under 1 yr.	Maclean	35	70 to 118
Cobliner *	9 to 21 days	Bertrand		Average 85
Mogwitz *	7 hr. to 3 wk.	Bang		70 to 103
Cannata *	1 to 24 hr.	Lewis-Benedict		70 to 100
Lucas and associates *	1 to 12 days	Folin-Wu		52 to 93

* Cited by Greenwald and Pennell.

BLOOD SUGAR VALUES IN CHILDREN

In 1915, Bass [7] reported on blood sugar levels of 60 children, using the Lewis-Benedict method. In his group there were 26 normal children and 34 nondiabetic abnormal children. Of the 26 normal subjects, 23 had blood sugar values ranging from 72 to 105 mg. per hundred cubic centimeters. There were 2 reports of a content level of 108 mg. per hundred cubic centimeters and 1 of 113 mg. The values for 30 of the 34 nondiabetic abnormal patients ranged between 60 and 105 mg. per hundred cubic centimeters. The average blood sugar value for his normal

5. Tisdall, F. F.; Drake, T. G. H., and Brown, A.: The Carbohydrate Metabolism of the Normal Infant, Am. J. Dis. Child. **30**:675 (Nov.) 1925.

6. Sedgwick, J. P., and Ziegler, M. R.: The Nitrogenous and Sugar Content of the Blood of the New-Born, Am. J. Dis. Child. **19**:429 (June) 1920.

7. Bass, M. H.: The Sugar Content of the Blood in Childhood, Am. J. Dis. Child. **9**:63 (Jan.) 1915.

subjects was 90 mg. per hundred cubic centimeters, and that for his non-diabetic abnormal patients 88.4 mg.

We are herewith reporting on a series of 144 children on whom we determined blood sugar levels both while they were fasting and at 11 a. m. From 9 to 12 subjects of each age group from 2 to 15 years, inclusive, were studied. Table 3 is a summary of the average values and the range of values for blood sugar for each age group, both while the subjects were fasting and at 11 a. m.

A study of table 3 convinces us that there is little, if any, change in blood sugar levels with the age group. The idea has been advanced by John [4] that there is a gradual but slight rise in the average blood sugar value in each decade of life, and his averages for decades 1 to 8

TABLE 3.—*Average and Range of Blood Sugar Values in Normal Children of Different Ages*

Age	Number of Subjects	Fasting Blood Sugar Values, Mg. per 100 Cc.		11 a. m. Blood Sugar Values, Mg. per 100 Cc.	
		Average	Range	Average	Range
2	10	79	66 to 104	87	76 to 105
3	9	82	74 to 93	79	70 to 91
4	10	80	70 to 92	86	72 to 104
5	12	88	75 to 94	86	77 to 94
6	10	87	80 to 95	81	70 to 94
7	9	85	70 to 105	85	75 to 98
8	9	88	82 to 95	92	83 to 115
9	12	91	83 to 102	84	52 to 93
10	12	91	84 to 104	87	73 to 101
11	9	88	76 to 93	84	77 to 107
12	9	93	85 to 98	92	84 to 97
13	11	93	83 to 101	85	67 to 93
14	10	91	61 to 110	89	80 to 100
15	12	87	84 to 95	84	71 to 96

are as follows: 91.8, 94, 96.4, 98, 100.9, 101, 102.7 and 107.4 mg. per hundred cubic centimeters. Our data may show a slight rise for the second decade over that for the first, but surely our averages are lower than his for both decades, and are close to the averages previously quoted for infants. Detailed study of our records reveals that only 2 values are above 105 mg. per hundred cubic centimeters, and those are among the determinations made at 11 a. m.; also, only 3 values are below 70 mg. per hundred cubic centimeters. Therefore, we feel justified in stating that levels for blood sugar fasting or at 11 a. m. in normal children practically always lie between 70 and 105 mg. per hundred cubic centimeters if obtained by the Folin-Wu method. It is not our purpose to introduce into this discussion reports on results from any other method, but since we frequently use the Folin-Malmros [8] micromethod in this

8. Folin, O., and Malmros, H.: An Improved Form of Folin's Micro Method for Blood Sugar Determination, J. Biol. Chem. **83**:115 (July) 1929.

clinic, we compared these two methods on bloods taken simultaneously from 12 patients both while they were fasting and at 11 a. m. and in constructing two blood sugar curves with values for specimens taken at two hour intervals. Charts 1 and 2 illustrate typical results from our use of the two methods. Results of the micromethod are less dependable

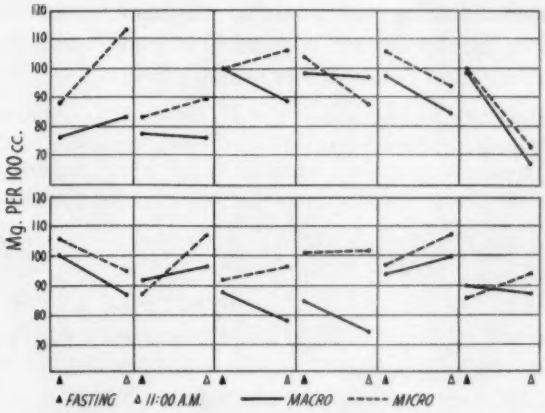

Chart 1.—Comparison of blood sugar values simultaneously determined by macromethod of Folin and Wu and by micromethod of Folin and Malmros.

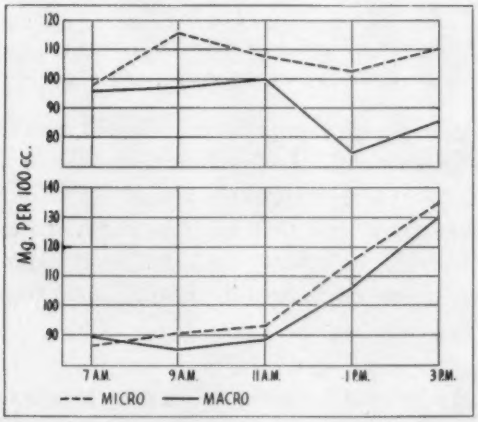

Chart 2.—Blood sugar curves obtained simultaneously by Folin-Wu and Folin-Malmros methods.

and, on the whole, the values are slightly higher than those obtained by the Folin-Wu method. By keeping these facts in mind we have been able to use the micromethod clinically with juvenile diabetic subjects.

Needless to say, we were surprised to find that in a majority of the subjects the 11 a. m. blood sugars were lower than the fasting sugars.

This difference was not wholly unexpected, but the frequency of its occurrence was not anticipated. Previous to the advent of insulin, it was common practice to give a diabetic patient orange juice one hour before breakfast to help him metabolize his food more readily. John [9] referred to this lowering of blood sugar levels after the ingestion of food as the "postprandial hypoglycemic dip," and Joslin, many years previously, had advocated taking advantage of the phenomenon as a means of attaining better dietary control of patients with diabetes. The following quotation from John [9] gives his explanation.

> This "post-prandial hypoglycemic dip" I think can be explained as being probably due to the primary stimulation of the insulogenic apparatus by the ingested food, with a consequent heavy outpouring of insulin which, so to speak, burns up more than the normal amount of sugar so that the hypoglycemia is produced.

Averages listed in table 4 illustrate the occurrence of this phenomenon in a majority of our subjects.

TABLE 4.—*Average Blood Sugar Values of One Hundred and Forty-Four Children*

Groups of Children	Number of Children	Value for Fasting Blood Sugar, Mg. per 100 Cc.	Value for 11 a. m. Blood Sugar, Mg. per 100 Cc.
Entire group	144	87.58	85.68
Children with postpoliomyelitic syndrome	17	86.24	88.79
Children with cerebral spastic paraplegia	12	83.00	84.53
Children with behavior problems	6	90.50	95.90
All children except those with postpoliomyelitic syndrome, cerebral spastic paraplegia and behavior problems	109	88.10	84.70

On further analysis of data we observed that those children listed as having a postpoliomyelitic syndrome, cerebral spastic paraplegia and behavior problems had a reversal of the average glycemic values, that is, a lower blood sugar at fasting than at 11 a. m. When we eliminate the data for these children, the average 11 a. m. blood sugar is 3.4 mg. per hundred cubic centimeters less than the fasting blood sugar.

COMMENT

Values for the normal amounts of fasting blood sugar find their greatest usefulness in the study and treatment of diabetes mellitus. Since slowly acting insulins have come into general use, there are more often needed definite figures for normal limits as a guide in therapy, particularly in the case of children in whom fluctuations from normal to abnormal are small. If one hopes to maintain a reasonably normal blood sugar level in a child, one must know the normal lower and upper

9. John, H. J.: A Study of 22,808 Blood Sugar Estimations, Fasting and Postprandial, in Non-Diabetic Individuals, Ann. Int. Med. **1**:470 (Jan.) 1928.

limits. The range of normal values in infants can safely be considered between 50 and 110 mg. per hundred cubic centimeters, but probably we more justly should place the limits at 60 and 100 mg. per hundred cubic centimeters, since practically all values are found to be within these limits. Levels for children between 2 and 15 years of age had the extreme range of 52 to 115 mg. per hundred cubic centimeters, but we have called attention to the fact that there were only 5 blood sugar values in 288 tests which did not fall between 70 and 105 mg. per hundred cubic centimeters. While an occasional value may be reported as slightly lower or slightly higher than these figures, it is a comparatively rare exception, since 98 per cent of our blood sugar values were between 70 and 105 mg. per hundred cubic centimeters. Furthermore, our reports indicate that blood sugar values determined three and one-half hours or longer after meals may be substituted for fasting blood sugar values in clinical practice. We use 11 a. m. blood sugar values and have found them satisfactory.

SUMMARY

Two hundred and eighty-eight blood sugar determinations were made by the Folin-Wu method on 144 nondiabetic children from 2 to 15 years of age, inclusive. Values for both fasting and 11 a. m. blood sugar were determined on the same day and the reports correlated.

There is no practical difference between fasting and 11 a. m. blood sugar values, since both fall within normal limits.

If the Folin-Wu method is used, normal fasting blood sugar values in nondiabetic children from 2 to 15 years of age range from 70 to 105 mg. per hundred cubic centimeters.

A review of the literature indicates that the range of normal blood sugar values in infants is probably 60 to 100 mg. per hundred cubic centimeters in most cases.

Clyde G. Culbertson, M.D., and Mrs. Gladys Phares, technician, gave counsel and technical help in the laboratory. Mrs. Phares made all blood sugar determinations.

Case Reports

POLYCYSTIC KIDNEY

REPORT OF A CASE STUDIED BY RECONSTRUCTION

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Because of the ease of its recognition, polycystic disease of the kidney has been of medical interest at least since the sixteenth century.[1]

Morgagni,[2] about a hundred years later, observed and described the "hydatids" which he found in several cadavers he had dissected. He noted that some of these "hydatids" were single, while others occurred as pairs or in larger numbers, and that some were "of the bigness of a small apple," while others were larger. Of 1 case he stated:

> Wherefore, although there were two other less hydatids, in other parts of the same kidney, they had not rais'd up that membrane beyond the surface of the kidney; that is to say, they were confin'd under it, like the other more frequent cells, and had hollow'd out a kind of bed for themselves, in the substance of the kidney. And a larger hydatid had, also, hollow'd out a seat for itself, in the upper part of the substance of this viscus, almost in the shape of a hemisphere; so that you might perceive it to be of the same kind with the others: the diameter of this hemisphere was equal to the breadth of a man's thumb.

Morgagni quoted, in addition, observations of similar "watry" abscesses from the writings of Harvey [3] and Willis.[4]

Since then, an extensive literature has accumulated, containing much speculation as to the cause of this peculiar and not uncommon condition. Several theories have been advanced concerning the mode of its origin, but since it is not a state which can be produced experimentally,[5] these theories have rested on the insecure ground of speculation and little

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From the Children's Memorial Hospital and the Otho S. A. Sprague Memorial Institute, Chicago.

1. Plater, F., cited by Krumbhaar, E. B.: Pathology: XIX. Clio Medica, a Series of Primers on the History of Medicine, New York, Paul B. Hoeber, Inc., 1937, pp. 46 and 163.

2. Morgagni, G. B.: The Seats and Causes of Diseases Investigated by Anatomy, translated from the Latin by B. Alexander, London, A. Millar & T. Cadell, 1769, vol. 2, pp. 320-322.

3. Harvey, W., cited by Morgagni,[2] p. 322.

4. Willis, T., cited by Morgagni,[2] p. 322.

5. Pettersson, A.: Ueber die Veränderungen der Niere nach Läsion der Papille beim Kaninchen, Beitr. z. path. Anat. u. z. allg. Path. **33**:605-620, 1903. Tollens: Ueber die Folgen der Markkegelobliteration der Kaninchenniere, Virchows Arch. f. path. Anat. **177**:477-485, 1904.

investigation. A recent case of polycystic disease of the kidney offered a remarkable opportunity to investigate further the pathogenesis of this disease.

REPORT OF CASE

Clinical Course.—N. H., a white girl, entered the Children's Memorial Hospital, Chicago, at the age of 5 months. Her family history was noncontributory, as was her own history except that she had failed to gain weight normally. A month before admission her abdomen was noticed to be distended, and a week later she became constipated. These symptoms increased in severity and were accompanied by anorexia.

Physical examination showed a weak, malnourished infant. The abdomen was distended, and both liver and spleen were enlarged. Separate from them were two hard, rounded and symmetric, bilateral masses extending from the flanks toward the pelvis; these masses were thought by Dr. Joseph Brennemann to be polycystic kidneys. The ribs were beaded and the costal borders flared.

The urine persistently showed traces of albumin and occasional casts and erythrocytes; there was moderate secondary anemia, which became increasingly severe. Results of tests for syphilis were negative, as were the reactions to the von Pirquet and Mantoux tests (with 0.1 and 1.0 mg. of tuberculin). Chemical studies of the blood six days after admission showed: nonprotein nitrogen, 61 mg. per hundred cubic centimeters; cholesterol, 194 mg.; uric acid, 5.1 mg.; creatinine, 2.5 mg. Eleven weeks later (one week before death) examination showed: nonprotein nitrogen, 55.6 mg.; creatinine, 1.6 mg.; calcium, 8.7 mg.; phosphorus, 6.7 mg., per hundred cubic centimeters.

The course was steadily downhill, with short febrile periods for which no cause could be found. The abdominal masses varied but little in size. On several occasions attempts were made to visualize the genitourinary tract by intravenous pyelography; although the bladder filled normally, the upper part of the urinary tract could not be seen, presumably because of a large amount of gas in the intestines. Three months after admission, bronchopneumonia developed, with death supervening a few days later.

Autopsy.—Necropsy was performed nine hours after death by Dr. Harold Roe. The anatomic diagnosis was: polycystic disease of both kidneys; malnutrition; bilateral lobular pneumonia; benign adenoma of the liver; fatty infiltration of the liver; patent ductus arteriosus.

Macroscopic Examination: The body was that of a pale, poorly developed and nourished girl; it weighed 3,500 Gm. and was 57 cm. long. No edema or subcutaneous fat was present. The head was of normal appearance and the anterior fontanel open. The chest was of the usual shape; the abdomen was markedly distended.

There were no adhesions or fluid in either pleural cavity; the pleural surfaces were smooth and glistening. Both lungs contained, posteriorly, small areas of lobular pneumonia. The heart, which weighed 35 Gm. (average weight for this age: 37 Gm.), was not remarkable; the ductus arteriosus was patent.

The peritoneal surfaces appeared normal; no free fluid or adhesions were present. The enlarged, blunt-edged liver extended 7 cm. below the costal margin and weighed 340 Gm. (average: 255 Gm.). Its capsule, which was everywhere smooth and shining, was a mottled, yellow brown. A solitary encapsulated tumor was visible externally in the posterior inferior portion of the left lobe, where it projected slightly above the surface of the surrounding hepatic tissue. When

Fig. 1.—External appearance of kidney, showing its increased size, swollen fetal lobulations and pale, cyst-spotted surface.

Fig. 2.—Median longitudinal section of kidney, the spongy, cystic cortex and normal medulla of which are clearly seen.

sectioned, this tumor was approximately 2.3 by 2.6 cm. in size; it was round and had a fibrous capsule. It was more yellowish than the hepatic tissue and was solid. The remaining portion of the cut surfaces consisted of swollen, brownish, fatty hepatic tissue. It was impossible to distinguish the finer hepatic structure with the naked eye.

The spleen was firm and considerably enlarged; it weighed 45 Gm. (average: 20 Gm.) and extended 2 cm. below the costal border.

Both kidneys were pale and symmetrically enlarged, each weighing 100 Gm. (average: 30 Gm.) and measuring 9.1 by 3.6 by 3.4 cm. Their capsules stripped easily, revealing smooth surfaces, on which the remains of fetal lobulations were still clearly visible. A peculiar feature of the kidneys, seen externally (fig. 1), was the peppering of the surface with minute, rounded, opaque areas which appeared dull and gray on the otherwise brown surface; these structures, when viewed by oblique light, projected slightly above the remaining cortical surface. They showed some individual variation in size, the largest being approximately 0.4 mm. in diameter. On section a remarkable appearance was met. The entire cortex was replaced by a honeycombed, spongy tissue (fig. 2), somewhat softer than that of the normal renal cortex. The differentiation between cortex and medulla was sharp, the latter appearing uninvolved. It was obvious from the cut surface that the honeycombing was caused by the presence of an extraordinary number of pinhead-sized cysts, all of which seemed to contain fluid. The medullary rays were somewhat swollen but were easily recognized, straight and undistorted. There were no scars. The calices were normal in appearance, as were the linings of the pelves, ureters and bladder. The major renal blood vessels showed no changes.

Microscopic Examination: There were small scattered areas of lobular pneumonia in both lungs.

The liver showed diffuse scarring in the neighborhood of the tumor. Elsewhere, aside from a moderate degree of fatty swelling, it was not remarkable. The tumor consisted of solid cords of liver cells which took a basophilic stain. There was no definite arrangement, the cords being chaotically placed. No mitotic figures were seen, nor were the tumor cells in any way anaplastic. They were supported by coarse, fibrous trabeculae, and the entire tumor mass was surrounded by a thick fibrous capsule; nowhere did the tumor extend beyond this capsule, which was fairly vascular. The entire appearance was that of a benign adenoma of the liver. The normal hepatic tissue immediately adjacent to it had undergone moderate atrophy from pressure.

The cortex of the kidney was almost completely replaced by a series of round or egg-shaped cysts (figs. 3 and 4). They gave the section a Swiss cheese appearance. Each of these cysts, when traced through serial sections, showed at one point or another a capillary tuft the appearance of which was identical with that of the ordinary glomerulus. The epithelium lining these cysts consisted of a single strand of flat cells; there were occasional areas near the poles of these cysts where the epithelium was thickened into several layers of cells. This thickening corresponded to the epithelial hyperplasia so frequently mentioned in the literature and may well represent the proximal convoluted tubule incorporated into its cystic glomerulus. Nowhere in any of the sections comprising this series could any connection between these cysts and definitely tubular structures be established. There were occasional noncystic glomeruli scattered through the cortex, especially in its more superficial portions; these appeared larger than normal, apparently

having undergone a compensatory hypertrophy in which the tubular portions shared. Otherwise the medullas and pelves were of normal appearance. The cortical cysts were supported by connective tissue, compressed, but in all other respects identical with that of the usual renal stroma.

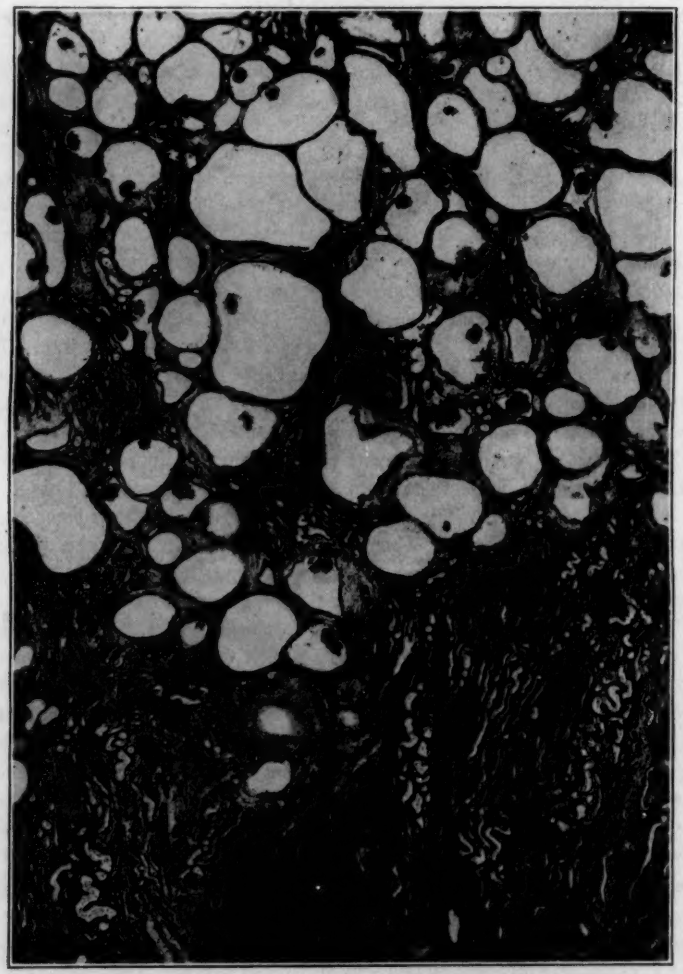

Fig. 3.—Photomicrograph (30 ×) of section of kidney (hematoxylin-eosin stain). Notice presence of glomerular capillary tufts in most of the cysts.

THE RECONSTRUCTION

Technic.—The kidneys were fixed in a solution of formaldehyde, and small blocks were taken from them. These blocks were dehydrated in 80 per cent, 95 per cent and absolute alcohols, then in absolute alcohol and ether (equal parts); embedded in 2, 4, 6 and 8 per cent solutions of celloidin (pyroxylin); blocked; hardened in chloroform vapor three hours; cut in perfect series at a thickness of 4 to 5 microns and stained with hematoxylin and eosin.

Sheets of white blotting paper [6] of standard weight were immersed in a bath consisting of a mixture of 5 parts of yellow wax U. S. P., 2 parts of paraffin and 1 part of rosin and then allowed to dry; the excess wax was then removed by scraping.

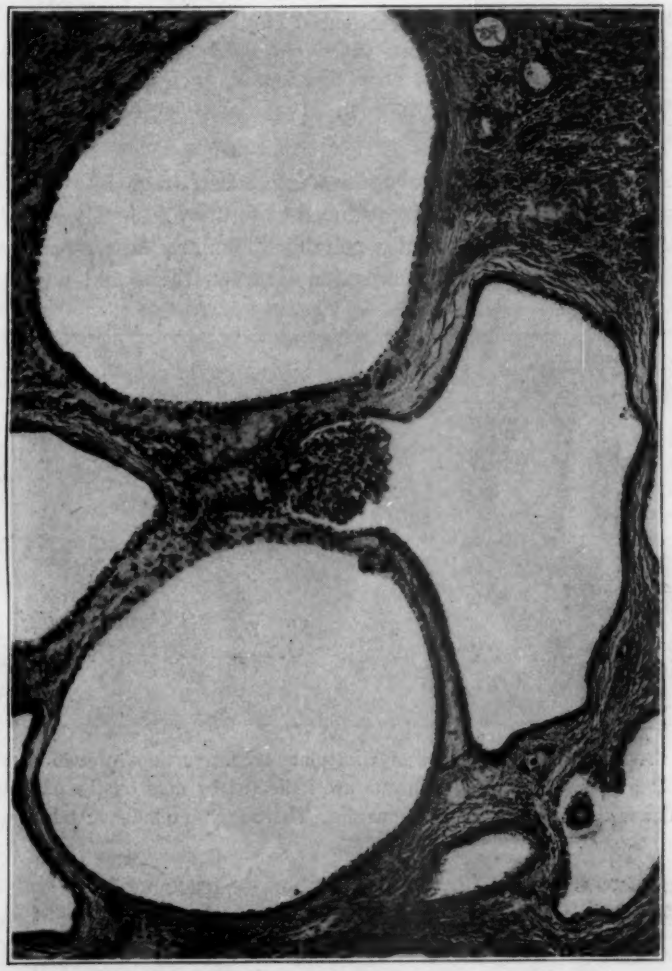

Fig. 4.—Photomicrograph (125 ×) of section of kidney (hematoxylin-eosin stain). This shows the finer structure of the glomerular cysts. Notice the "epithelial hyperplasia."

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6. Gage, S. P.: The Method of Making Models from Sheets of Blotting Paper, Anat. Rec. **1**:166-169 (Nov. 10) 1907. Miller, W. S.: The Use of Blotting-Paper for Reconstructions, ibid. **48**:191-196 (Jan. 25) 1931. Strong, R. M.: Cardboard for Anatomic Reconstruction Models, Science **83**:39-40 (Jan. 10) 1936.

The sections were projected by means of a projection microscope directly onto Eastman bromide paper P. M. C. no. 2 (lightweight, matte finish) at a uniform magnification of 100 diameters. After having been developed, fixed and dried, these magnified prints were flattened.

The various structures for reconstruction were identified in the successive prints in which they appeared and then traced on the blotting paper wax plates by means of a stylus and lightweight carbon paper. After having been thus traced, the sections were cut from the wax plates [7] and, after proper orientation, stacked. The resulting models, with the position of the glomerular tufts marked on the external surfaces, were then drawn.

Interpretation.—Several cysts were reconstructed by the method described. Two of them are reproduced in figure 5.[8] As shown in these illustrations, the cysts assumed a roughly globular shape. An exacting search failed to reveal any connection between them and any tubular

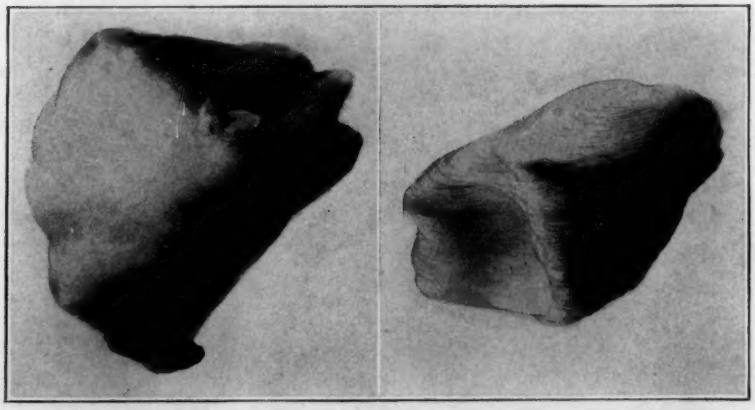

Fig. 5.—Exact scale drawings of wax plate reconstructions of two glomerular cysts. Sites of glomerular attachments are indicated by dots on the external surfaces. The irregularity of shape is apparent. There are no tubular attachments.

components. It was, however, possible to trace such a connection between some normal glomeruli and their proximal convoluted tubules.

On examination, therefore, these plastic models were without any efferent connections. Hence, it is reasonable to assume that such glomerular cysts originated because of a failure of the glomerular and the tubular elements of the nephron to unite.

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7. Born, G.: Die Plattenmodellirmethode, Arch. f. mikr. Anat. **22**:584-599, 1883; Noch einmal die Plattenmodellirmethode, Ztschr. f. wissensch. Mikr. **5**: 433-455, 1888.

8. The cost of making these drawings was defrayed by a grant from the Rockefeller Foundation to the department of anatomy of the University of Chicago.

The capillaries must have grown normally into the glomeruli, which as a consequence assumed an excretory, filtering function and finally, because of the inevitable retention, a cystic character. The supporting and connecting tissue between these cysts was compressed by their growth.

THEORIES OF THE FORMATION OF MULTIPLE RENAL CYSTS

It may be valuable to review briefly the theories concerned with the pathogenesis of cysts of the kidney. The extensive literature which had accumulated up to 1913 was admirably surveyed by Berner,[9] to whose monograph the interested reader is directed.

There seems to be no disagreement that multiple renal cysts are congenital. Virchow[10] at first thought that those which he found in adults had been acquired, whereas those of the newborn were of congenital origin. While some of his contemporaries[11] agreed with this idea, Virchow himself later abandoned it.

It was Virchow[10] who formulated the retention, or papillitis, theory: After an interstitial inflammatory process, there is proliferation of stroma sufficient to cause atresia of the tubular papillae, with resultant tubular occlusion. The latter could also occur from accumulation of intratubular detritus, salts and cells. Von Mutach,[12] however, probed the papillae of cystic kidneys and showed them to be patent. Hanau[13] was unable to find the interstitial inflammation postulated by Virchow; he concluded, on the basis of careful studies, that there was an aplasia of the papillae, due to a defect of their anlage (*Anlagefehler*).

Others subscribing to this theory were Wigand,[14] Marchand,[15] Lust,[16] Stieda[17] and Witte.[18] Witte expressed the belief that "papillitis

9. Berner, O.: Die Cystenniere: Studien über ihre pathologische Anatomie, Jena, Gustav Fischer, 1913.

10. Virchow, R.: Ueber Hydrops renum cysticus congenitus, Virchows Arch. f. path. Anat. **46**:506, 1869.

11. Jacob, P.: Ueber Hydrops renum cysticus; klinischer Theil, Charité-Ann. **25**:16-22, 1900. Davidsohn, C.: Ueber Hydrops renum cysticus; pathologisch-anatomischer Theil, ibid. **25**:22-27, 1900.

12. von Mutach, A.: Beitrag zur Genese der congenitalen Cystennieren, Virchows Arch. f. path. Anat. **142**:46-86, 1895.

13. Hanau, L.: Ueber congenitale Cystennieren, Giessen, C. von Münchow, 1890.

14. Wigand, F.: Ueber congenitale Cystennieren (Cystenbildung durch Retention und cystische Degeneration), Marburg, R. Friedrich, 1899.

15. Marchand: Ueber die Beziehungen der pathologischen Anatomie zur Entwickelungsgeschichte, besonders der Keimblattlehre, Verhandl. d. deutsch. path. Gesellsch. (1899) **2**:38-105, 1900.

16. Lust, W.: Ueber angeborene Nieren- und Lungencysten, Leipzig, M. Hoffmann, 1895.

(Footnotes continued on next page)

fibrosa" was present; using serial sections, he found tubular connections with most glomerular cysts, which he nevertheless attributed to retention.

The second attempt to explain this condition was made by Brigidi and Severi.[19] They expressed the belief that these renal cysts were neoplastic, analogous to ovarian cystadenomas. Further support was lent to this belief by the work of Nauwerck and Hufschmid,[20] who were attracted to the epithelial cellular nests (*Sprossen*) in the renal tubules. Von Kahlden,[21] about the same time, studied material from 2 cases of cystic liver and kidney in adults and concluded from the epithelial cell groups which he observed growing into the renal stroma that the underlying process was neoplastic. In the material from a third case,[22] he asserted that the cysts were analogous to intracanalicular fibroadenoma of the breast.

Borst,[23] who subscribed to the monistic theory of renal embryonic development, expressed the belief that the primary disturbance in cystic disease of the kidney is an imbalance between epithelium and stroma, resulting in unregulated epithelial growth into the connective tissue. He concluded that such epithelial sprouts dilate into cysts because of increased cellular proliferation and adenomatous secretion.

The theory which meets with most support at present has developed from increasing knowledge of renal embryology.[24] At first it was thought that the kidney had a monistic origin, that is, that ureter, pelvis, tubules and glomeruli were all derived from the wolffian duct. More recent investigation of renal embryogenesis has shown this monistic theory to be in error. Schreiner [25] and other embryologists have proved

17. Stieda: Zur Entstehung der Cystennieren, Centralbl. f. allg. Path. u. path. Anat. **12**:532-537, 1901.

18. Witte, P.: Erworbenes multiloculäres Adenokystom und angeborene cystische Entartung der Nieren, Königsberg, E. Rautenberg, 1896.

19. Brigidi, V., and Severi, A.: Contributo alla patogenesi delle cisti renale, Sperimentale **46**:1-25, 1880.

20. Nauwerck, C., and Hufschmid, K.: Ueber das multiloculäre Adenokystom der Niere, ein Beitrag zur Kenntnis der Cystennieren, Beitr. z. path. Anat. u. z. allg. Path. **12**:1-28, 1892.

21. von Kahlden, C.: Ueber die Genese der multiloculären Cystenniere und der Cystenleber, Beitr. z. path. Anat. u. z. allg. Path. **13**:291-308, 1893.

22. von Kahlden, C.: Ueber ein congenitales Adenom beider Nieren, Beitr. z. path. Anat. u. z. allg. Path. **15**:626-632, 1894.

23. Borst, M.: Die Lehre von den Geschwülsten, mit einem Atlas, Wiesbaden, J. F. Bergmann, 1902.

24. Huber, G. C.: Renal Tubules, in Cowdry, E. V.: Special Cytology: The Form and Functions of the Cell in Health and Disease, ed. 2, New York, Paul B. Hoeber, Inc., 1932, vol. 2, pp. 935-977. Keibel, F., and Mall, F. P.: Manual of Human Embryology, Philadelphia, J. B. Lippincott Company, 1910.

25. Schreiner, K. E.: Ueber die Entwicklung der Amniotenniere, Ztschr. f. wissensch. Zool. **71**:1-189, 1902; Om udviklingen af amnioternes blivende nyre og dennes forhold til urnyren, Norsk mag. f. lægevidensk. **63**:292-324, 1902.

the double origin of the kidney: that the ureter, pelvis and tubules, except in their proximal convoluted portions, evolve from the wolffian duct, whereas these proximal convoluted tubules and the glomeruli arise from the nephrogenic blastema. These two independently derived elements are subsequently united (fig. 6).

Reasoning from the theory of the dualistic origin of the kidney, Hildebrand [26] concluded that renal cysts occur because of a failure of the two components to join, that this nonunion causes a retention of fluid and consequent cystic formation in the glomerular portions and that the formation of the resultant cysts ultimately depends on this developmental malformation.

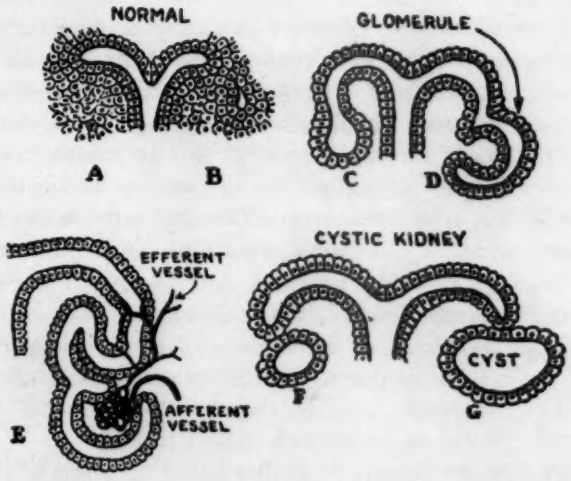

Fig. 6.—Formation of the glomerulus. In *E*, ingrowth of the vascular tuft is indicated. *F* and *G* illustrate the prevailing theory of etiology in polycystic renal disease, viz., failure of union between the excretory and the collecting elements of the renal tubules (from Campbell, M. F.: Pediatric Urology, New York, The Macmillan Company, 1937, vol. 1, p. 184).

Springer,[27] who likewise subscribed to the dualistic theory of renal development, stated the belief that when these two anlages fail to join it is because of an interposing interstitial proliferation.

Ribbert [28] stated that the concept of a dualistic renal origin is of particular significance in the understanding of cystic kidney. He cited the

26. Hildebrand: Weiterer Beitrag zur pathologischen Anatomie der Nierengeschwülste, Arch. f. klin. Chir. **48**:343-371, 1894.

27. Springer, J.: Ein weiterer Beitrag zur Genese der Cystennieren, Zurich, J. Schabelitz, 1897.

28. Ribbert, H.: Uber die Entwickelung der bleibenden Niere und die Entstehung der Cystenniere, Verhandl. d. deutsch. path. Gesellsch. (1899) **2**:187-201, 1900.

case of a newborn boy with bilateral cystic kidneys. His description of these kidneys makes me feel that they were probably identical with those of the infant whose case I have described. Ribbert found that a majority of these cysts contained glomeruli; he expressed the opinion that those which did not had their origin in the tubular portions of the kidney, thus ascribing a secretory function to the tubular elements of the kidney. He did not consider the possibility that these aglomerular cysts might have been of lymphatic character. Ribbert, like Springer,[27] concluded that the nonunion was due to an abnormal increase of connective tissue. He was emphatic in holding that all cystic kidneys have a common cause and that those of both early and later life depend on an identical process.

Von Mutach,[12] too, stated that the cause was a developmental anomaly. He studied some 40 cysts by means of thick serial sections and found that these cysts were connected with tubules; he concluded that they were glomerular, as he found an arteriole leading to each. He discovered that such tubules, with deformed blind ends, as connected with the cysts, stained differently from the normal renal tubules.

Herxheimer[29] also subscribed to the malformation theory. He expressed belief not in an inflammatory basis but rather in a fundamental developmental imbalance between epithelial and connective tissue structures.

Jägerroos,[30] another dualist, asserted that it was inadequate to explain cysts of the kidney as a malunion of the two anlages; he concluded that the cysts were due to a tendency of the interstitial tissue to form its fibers abnormally, that is, that the fibers, instead of running parallel to the tubules, encircled and choked them.

There are but few reports of studies based on serial sections,[31] and only occasional references to reconstructions of renal cysts by the use of camera lucida drawings.[32]

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29. Herxheimer, G.: Ueber Cystenbildungen der Niere und abführenden Harnwege, Virchows Arch. f. path. Anat. **185**:52-117, 1906; Ueber hyaline Glomeruli der Neugeborenen und Säuglinge: Ein Hinweis auf die Häufigkeit entwicklungsgeschichtlicher Irrungen und deren Beziehungen zur Geschwulstlehre, Frankfurt. Ztschr. f. Path. **2**:138-152, 1908-1909.

30. Jägerroos, B. H.: Zur Kenntnis der Zystenbildungen und der normalen Entwicklung der Niere, Arb. a. d. path. Inst. d. Univ. Helsingfors **2**:1-90, 1908.

31. Bunting, C. H.: Congenital Cystic Kidney and Liver with Family Tendency, J. Exper. Med. **8**:271-288, 1906. Beeson, H. G.: Polycystic Disease in a Premature Infant, J. Urol. **30**:285-298 (Sept.) 1933. von Mutach.[12] Witte.[18]

32. Hauch, E.: Ueber die Anatomie und Entwickelung der Nieren, Anat. Hefte **22**:153-248 (May) 1903. Stoerck, O.: Beitrag zur Kenntnis des Aufbaus der menschlichen Niere, ibid. **23**:283-328, 1904. Huber, G. C.: On the Development and Shape of Uriniferous Tubules of Certain of the Higher Mammals, Am. J. Anat. (supp.) **4**:1-98, 1904-1905. Meader, F. M.: A Study of the Anatomical Relations in a Congenital Cystic Kidney, Bull. Johns Hopkins Hosp. **18**:354-355 (Sept.) 1907. Schreiner.[25] Berner.[9]

To the best of my knowledge, the study reported in this paper is the first to be made with a photographic, plastic reconstruction technic. I believe it offers incontrovertible evidence in favor of the theory that, as in the case cited, the development of multiple renal cysts depends on a failure of the two anlages of the kidney to unite. It is impossible to recognize the fundamental causative factors of this nonunion. The presence of another congenital anomaly, a hepatic adenoma, in the patient reported on suggests a widespread developmental disturbance which may be attributed to "defective germ plasm," as does the frequent coexistence of congenital cystic liver with congenital cystic kidney.

SUMMARY

The clinical course and observations at autopsy on an 8 month old girl with bilateral cystic disease of the kidneys have been described.

The technic by which these kidneys were studied and the wax plate models constructed has also been described.

The three main theories which attempt to explain the cause of this condition have been reviewed.

The total lack of connection between these cysts and any tubules has been commented on and ascribed to a nonunion of the two renal anlages.

This study, therefore, lends further support to the belief that cystic disease of the kidney commonly arises as a developmental anomaly whereby the glomeruli fail to unite with the tubules and become distended by the secretion from their glomerular tufts.

115 East Seventy-Second Street.

MALIGNANT HYPERTENSION IN A CHILD

CURE FOLLOWING NEPHRECTOMY

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AND

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ROCHESTER, MINN.

The work of Goldblatt and his associates,[1] as well as that of others, has focused attention on the role of ischemia of the kidneys, and particularly on the role of ischemia of a single kidney in the production of arterial hypertension. After this experimental work, attempts have been made to correct hypertension in patients in whom disease has resulted in destruction of a major portion of one kidney. In these attempts nephrectomy has been carried out chiefly because of the presence of hypertension rather than because of the existence of any other indication for surgical treatment.

In 1937, Butler[2] made a study of the relation of hypertension to pyelonephritis in children. He studied the records of 15 cases in which the patients were 3 to 11 years of age and in which evidence of pyelonephritis had been demonstrated at necropsy. Records of the blood pressures were inadequate in 7 of the cases. In the other 8 cases the average blood pressure was 190 mm. of mercury systolic and 140 mm. diastolic. Hypertensive crises occurred in 2 of these cases, and the patients died before any evidence of renal impairment appeared. In 2 other cases pyelonephritis and hypertension preceded severe retention of nitrogen.

Thus, Butler studied 15 cases in which children had had pyelonephritis and hypertension for a period of years before appreciable diminution of renal function occurred. Six of the children had died before he made his report. He presented detailed records of 6 cases. In the first case studied the sequence of events was pyelonephritis, hypertension, resection of the splanchnic nerve, uremia and death. Permission for

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From the Section on Pediatrics (Dr. Kennedy) and the Divisions of Medicine (Dr. Barker) and Surgery (Dr. Walters) of the Mayo Clinic.

1. Goldblatt, H.; Lynch, J.; Hanzal, R. F., and Summerville, W. W.: Studies on Hypertension: I. The Production of Persistent Elevation of Systolic Blood Pressure by Means of Renal Ischemia, J. Exper. Med. **59**:347 (March) 1934.

2. Butler, A. M.: Chronic Pyelonephritis and Arterial Hypertension, J. Clin. Investigation **16**:889 (Nov.) 1937.

necropsy was not obtained. In the second case there had been an infection of the urinary tract and symptoms suggesting hypertension of eighteen months' duration. Further study could not be made, because the patient had been removed from the hospital against advice. In the third case the development of pyelonephritis was followed by hypertension, cardiac failure and death. Necropsy revealed cardiac hypertrophy, sclerosis of the aorta, bilateral pyelonephritis, bilateral hydronephrosis, arteriolar sclerosis and cystitis. In the fourth case bilateral pyelonephritis, hypertension and cardiac decompensation were present. At necropsy, bilateral pyelonephritis, cardiac hypertrophy and arteriolar sclerosis of the kidneys, pancreas, spleen and periadrenal tissues were found. In another case the patient had had a ureteral calculus and unilateral pyelonephritis. In eight months hypertension and signs of cardiac failure had developed. Nephrectomy was followed by return of the blood pressure to normal for twenty months.

In a case reported in detail by Barney and Suby [3] the patient had had pyelitis for two years. The blood pressure was 190 mm. of mercury systolic and 122 mm. diastolic. It was determined that the renal involvement was unilateral. Nephrectomy was followed by a fall in the blood pressure to 92 mm. of mercury systolic and 60 mm. diastolic. The blood pressure remained normal after twenty months.

Butler demonstrated that in children pyelonephritis, either bilateral or unilateral, may be accompanied by arterial hypertension, and in 2 instances (in 1 patient whom he observed personally and in another reported on by Barney) removal of the one pyelonephritic kidney was followed by return of an elevated blood pressure to a normal level. His description of the pathologic changes found in the kidneys, removed at operation and at necropsy, is similar to that given by others. The changes consist chiefly in sclerosis and round cell infiltration, resulting from inflammation, great narrowing of the arterioles and smaller arteries and a great reduction in the amount of normal renal tissue.

Barker and Walters,[4] in 1938, reported the case of a man aged 42 who had suffered from right ureteral calculus and infected hydronephrosis on the right side. Chronic atrophic pyelonephritis subsequently developed in the right kidney after the removal of the ureteral calculus. Hypertension was known to have developed after the kidney had undergone considerable contraction. The blood pressure at the time the patient was admitted to the hospital was 232 mm. of mercury

3. Barney, J. D., and Suby, H. I.: Unilateral Renal Disease with Arterial Hypertension: Report of a Case Apparently Cured Following Nephrectomy, New England J. Med. **220**:744 (May 4) 1939.

4. Barker, N. W., and Walters, W.: Hypertension Associated with Unilateral Chronic Atrophic Pyelonephritis: Treatment by Nephrectomy, Proc. Staff Meet., Mayo Clin. **13**:118 (Feb. 23) 1938.

systolic and 135 mm. diastolic. After nephrectomy the blood pressure fell to 130 mm. of mercury systolic and 90 mm. diastolic and has remained at approximately these levels for two years. Since then they have carried out operations on 3 other patients,[5] aged from 35 to 52 years, who had hypertension associated with unilateral chronic atrophic pyelonephritis. In each instance the blood pressure has fallen to levels considered within normal limits and has remained at these levels.

We wish to report in detail the case of a girl, aged 7 years, who had severe hypertension associated with severe retinitis and papilledema, typical of the retinitis of malignant hypertension (Wagener and Keith [6]). Following nephrectomy, there was a remarkable return of blood pressure to normal with disappearance of retinitis.

REPORT OF A CASE

A girl aged 7 years was registered in the Section on Pediatrics of the Mayo Clinic Oct. 3, 1939 because of headaches, high blood pressure and "kidney trouble." Except for the fact that the mother had suffered from hypertension during pregnancy, the family history was irrelevant. The child's birth had been normal and her development had proceeded without incident. There were 5 siblings, 1 of whom had had pyelitis at 10 years of age.

At 2 years of age the patient had begun to experience spells of sickness, which had consisted of general malaise and headache and had lasted from a few minutes to a day. These spells had occurred only occasionally at first, but during the year before the patient was observed at the clinic they had become increasingly more frequent, and for the three weeks preceding her admission they had been present almost constantly.

It was said that the findings in urinalyses, made during the previous two years, had been abnormal, but more detailed information was not obtained. During early childhood she had suffered from enuresis. This had ceased, but at the time of her admission nocturia was present and she had to micturate one or two times each night. There had been occasional frequency of micturition during the day.

Ten months before her admission she had suffered from a severe form of measles. Urinalysis at that time had revealed albuminuria. Her systolic blood pressure at that time was said to have been 180 mm. of mercury. She had been kept in bed for five months. At the end of that time, her tonsils and adenoids had been removed. After this procedure she had been free from headaches for about a month.

Three months before her admission the headaches had recurred, and rest in bed had been advised. She had not had any bleeding, pruritus, vomiting or vertigo. Five weeks before her admission the right eye had turned inward. A few days before her admission she complained of blurring of vision when she looked at objects with her right eye. Her appetite had remained good. Her general condition had been considered good. There was never any edema, but for a few weeks she had complained at times that her hands and feet went to sleep.

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5. Barker, N. W., and Walters, W.: Hypertension and Chronic Atrophic Pyelonephritis: Results of Nephrectomy, J. A. M. A. **115**:912 (Sept. 14) 1940.

6. Wagener, H. P., and Keith, N. M.: Diffuse Arteriolar Disease with Hypertension and the Associated Retinal Lesions, Medicine **18**:317 (Sept.) 1939.

Physical examination revealed a girl rather small for 7 years of age. Her height was 45 inches (114.3 cm.), and she weighed 40 pounds (18.1 Kg.). She did not appear to be ill. The left border of the heart appeared to be outside the left mamillary line. The heart sounds were strong and forceful. The second aortic sound was markedly accentuated. Palpation revealed that the peripheral arteries were firm and slightly tortuous.

Examination of the ocular fundi revealed: general narrowing, grade 3 to 3 plus (on the basis of 4), of the retinal arterioles; sclerosis, grade 1, of the chronic type, and localized angiospastic narrowing, grade 3, in some arterioles, especially in the right inferior temporal arteriole. Other changes noted were extensive retinitis of the malignant hypertensive type[6] (group 4), hyperemia and edema of the disks of 5 D., cotton wool patches, hemorrhagic extravasations and heavy star formation on the macula. The right external rectus muscle was weak (grade 2); right convergent strabismus and homonymous diplopia, which was greater toward the right side, also were present.

The specific gravity of the urine was 1.008. Urinalysis disclosed albuminuria, grade 2 on a basis of 1 to 4, and an occasional pus cell. Sugar was not present

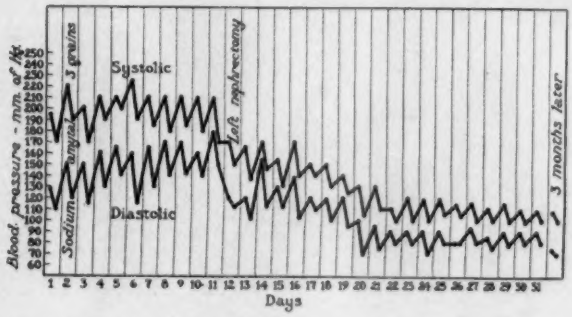

Fig. 1.—Graphic representation of the systolic and diastolic blood pressure determined before and after removal of the left kidney; the blood pressure was taken hourly, but only the highest and lowest values for each day were used in constructing this graph; one should note the values for the blood pressures taken three months after the operation.

in the urine. The value for the hemoglobin was 14.4 Gm. per hundred cubic centimeters of blood. The results of a flocculation test for syphilis and of tuberculin tests were negative. A roentgenogram of the thorax showed that the arch of the aorta was prominent and somewhat tortuous.

The child was admitted to the hospital for further study. Hourly blood pressure readings were made with the child at rest in bed. The blood pressure varied from 225 mm. of mercury systolic and 178 mm. diastolic to 170 mm. systolic and 110 mm. diastolic. Following the administration of 3 grains (0.2 Gm.) of sodium amytal by mouth, there was no material change in the level of either the systolic or the diastolic blood pressure. Although the child was at rest in bed, the level of the blood pressure continued to be about the same as it had been (fig. 1). During the application of the cold pressor test[7] the blood pressure rose to 230 mm. of mercury systolic and 180 mm. diastolic.

7. Hines, E. A., Jr.: Reaction of the Blood Pressure of Four Hundred School Children to a Standard Stimulus, J. A. M. A. **108**:1249 (April 10) 1937.

The concentration of urea was 18 mg. per hundred cubic centimeters of blood; the value for the serum calcium was 11.2 mg. per hundred cubic centimeters, and that for the serum phosphorus was 3.2 mg. per hundred cubic centimeters. An excretory urogram revealed an apparently normal right kidney. There was a question whether the left kidney excreted any of the opaque medium. Cystoscopic examination revealed a normal bladder, but there was edema, grade 1, of the left ureteral orifice. No spurts of urine could be seen on the left, but the spurts were normal on the right side. A bilateral retrograde pyelogram revealed a normal right kidney, pelvis and ureter. The left renal pelvis was apparently small and dilated; the calices were abbreviated, clubbed and cicatricial. This picture suggested chronic atrophic pyelonephritis (fig. 2).

On Oct. 13, 1939 the left kidney was removed by one of us (W. W.). It was approximately 2.5 by 3.5 cm., and there was hydronephrosis of equal degree. A small blood vessel, a few millimeters in size, crossed the ureteropelvic juncture. This was thought to be responsible for the hydronephrosis.

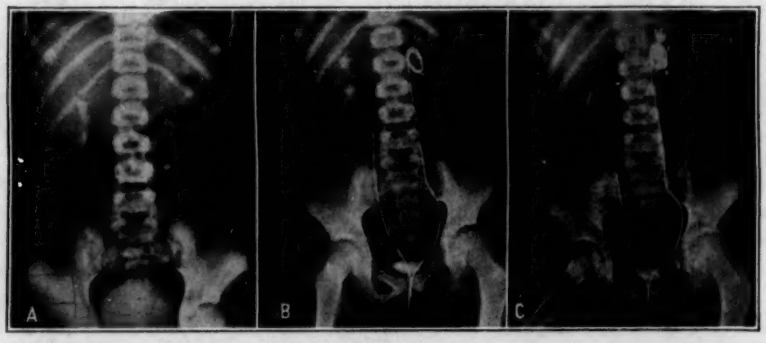

Fig. 2.—*A*, excretory urogram, and *B* and *C*, retrograde pyelograms, showing normal outline of the right kidney and dilatation of the pelvis of the left kidney with short, clubbed calices, indicative of atrophic pyelonephritis.

Pathologic examination of the specimen revealed that its weight was 9 Gm. The microscopic diagnosis was pyelonephritis, grade 3. Most of the glomeruli were grouped closely together, and approximately 95 per cent of them were fibrotic and partially or completely hyalinized. The tubules were atrophic, and many contained casts. The blood vessels showed marked thickening of the walls; in many vessels there was obliteration of the lumen (fig. 3).

The blood pressure obtained as soon as the patient returned from the operating room was 156 mm. of mercury systolic and 100 mm. diastolic. The next day it was 134 mm. of mercury systolic and 100 mm. diastolic. From that time there was a gradual decrease of the blood pressure until about the eighth or ninth day after operation, when it reached 110 mm. of mercury systolic and 85 mm. diastolic. At this time the cold pressor test produced a rise in the blood pressure to 170 mm. of mercury systolic and 140 mm. diastolic. On the seventeenth postoperative day it was possible to raise the blood pressure to only 140 mm. of mercury systolic and 104 mm. diastolic with the cold pressor test.

Five days after operation examination of the ocular fundi showed no particular change. Starting at about the tenth day after operation and continuing thereafter, there were progressive recession of the edema of the optic disks, decrease in the amount of arteriolar spasm and clearing up of the exudates and hemorrhages. The patient was permitted to return home, after an uneventful convalescence.

Three months after operation she was reexamined. She had been feeling well, and there had been no return of headaches. The strabismus had corrected itself, and she had gained 8 pounds (3.6 Kg.). The blood pressure at that time was as follows: left arm, 108 mm. of mercury systolic and 74 mm. diastolic; right arm, 102 mm. of mercury systolic and 70 diastolic. There was no rise in blood pressure during the application of the cold pressor test. The examination of the eyes

Fig. 3.—Photomicrograph of tissue of left kidney; most of the kidney presented this appearance, with marked sclerosis, destruction of the glomeruli and tubules and marked thickening of the walls of the smaller arteries and arterioles, with diminution of the caliber of the lumens (× 80).

revealed vision of 6/5 in the right and 6/6 in the left. The pupils, reflexes and visual fields were normal. The retinal arterioles were generally narrowed, grade 1 to 1 plus, and there was minimal sclerosis of chronic type. There was no visible localized active spasm or postspastic sclerosis. The examination revealed exudates residual to the previous edema, some of which were deep and plaquelike, scattered in and about the macula of the retina. There was slight increase of residual connective tissue on the optic disks. The disks were flat; no active retinal lesions were seen. It appeared from this examination that there was evidence of excellent recovery.

COMMENT

As evidence of cure, the appearance of the ocular fundi before and after operation is of especial interest. Before operation the findings in the ocular fundi were those of acute angiospastic retinitis, similar to that seen in association with malignant hypertension. Shortly after operation the changes in the ocular fundi had subsided to a point at which the ophthalmologist could state with confidence that complete recovery was assured.

When this patient was first seen and examined it appeared that the prognosis was hopeless. Patients with similar vascular findings, such as some of those in the cases reported by Amberg,[8] have been followed, and it was found that death occurred within a relatively short time after onset of the hypertension. With the finding of unilateral atrophic pyelonephritis in the case which we have reported, hopes were entertained that some benefit might follow nephrectomy, such as took place in the individual cases reported by Butler and by Barney, but the recommendation that nephrectomy might be of benefit was made as a measure of desperation. The apparent complete cure of malignant hypertension by the relatively simple procedure of nephrectomy should constitute a valid reason for a urologic examination in every case of malignant hypertension in which the patient is a child. If definite unilateral renal disease is found, nephrectomy should be accorded prime consideration as a therapeutic measure.

SUMMARY

A patient aged 7 years who had clinical evidence of malignant hypertension has been clinically cured for three months by the removal of a kidney which as a result of obstruction and infection had become atrophic.

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8. Amberg, S.: Hypertension in the Young, Am. J. Dis. Child. **37**:335 (Feb.) 1929.

Progress in Pediatrics

CONGENITAL INTESTINAL OBSTRUCTION

WITH SPECIAL REFERENCE TO THE VALUE OF THE PLAIN ROENTGENOGRAM FOR DIAGNOSIS

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The prognosis for congenital intestinal obstruction has changed materially since 1927. Prior to this date, authorities were unanimous in predicting an almost uniformly fatal outcome after a brief illness.[1] In view of the fact that previously only 4 patients were known to have survived, this estimate of the mortality was an understatement. Since that date, reports of increasing numbers of patients successfully treated surgically have led both pediatricians and surgeons to recommend, with some optimism, immediate surgical intervention in cases of congenital obstruction of the bowel.

The first successful operations were performed in 1897,[2] 1910,[3] 1916,[4] 1924[5] and 1926.[6] In 1927 there were reports of a number of similarly fortunate operative results.[7] Since that year, equally happy reports have

From the Departments of Pediatrics and Radiology of the Beth Israel and Jewish Maternity Hospitals.

1. Finkelstein, H.: Lehrbuch der Säuglingskrankheiten, Berlin, Julius Springer, 1924, pp. 707-709. von Reuss, A. R.: Diseases of the Newborn, New York, William Wood & Company, 1920, pp. 225-260. Holt, L. E.: Diseases of Infancy and Childhood, ed. 7, New York, D. Appleton and Company, 1916, p. 118. Grulee, C. G., and Bonar, B.: The Newborn: Diseases and Abnormalities, in Haynes, R. S.: Clinical Pediatrics, ibid., 1926, vol. 3, pp. 145-151. Thorndyke, A.: Duodenal Atresias and Stenoses in Infancy, Boston M. & S. J. **196**:763, 1927.

2. Rogers, E.: Successful Operation for Intestinal Obstruction in an Infant Sixty-Four Hours Old, Tr. Colorado S. M. Soc., 1897, p. 422.

3. Fockens, P.: Ein operationgeheilter Fall von kongenitaler Dünndarmatresie, Zentralbl. f. Chir. **38**:532, 1910.

4. Ernst, N. P.: A Case of Congenital Atresia of the Duodenum Treated Successfully by Operation, Brit. M. J. **1**:644, 1916.

5. Richter, H. M.: Surgery of the Gastrointestinal Tract in Children, in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1924, vol. 3, p. 512.

6. Bolling, R. W.: Complete Congenital Obstruction of the Duodenum: Duodeno-Jejunostomy at Nine Days of Age, Ann. Surg. **83**:543, 1926.

7. (*a*) Loitman, C.: Congenital Occlusion of the Intestine: Report of Four Cases, Boston M. & S. J. **197**:21, 1927. (*b*) MacLennan, A.: Acute Intestinal Obstruction in Infancy and Childhood, Brit. M. J. **2**:818, 1927. (*c*) Sweet, G. B., and Robertson, C.: Case of Congenital Atresia of Jejunum, Arch. Dis. Childhood **2**:186, 1927. (*d*) Weeks, A., and Delprat, G. D.: Congenital Intestinal Obstruction, S. Clin. North America **7**:1193, 1927.

appeared at not infrequent intervals. Loitman,[7a] in 1927, and Webb and Wangensteen,[8] in 1931, were the first to sound an encouraging note concerning the treatment of congenital intestinal atresia. The latter authors reviewed more than 500 cases; they mentioned the fact that not all cases have been recorded and that previously a lethal ending was the expected and awaited result. They reported 17 cases, 13 of atresia and 4 of stenosis; 2 of their patients survived as a result of successful surgical intervention. In 1933 Ladd[9] reported 60 cases, the largest series on record, in 40 of which the condition was due to intrinsic lesions and in 20 to anomalies of intestinal rotation. Seventeen of the 60 patients were relieved by operation, a recovery rate of 28 per cent, which is a considerable improvement over the rate previously estimated as 1 per cent. Ladd also cited 29 cases previously reported in the literature in which operation was successful. Cole, in discussing Ladd's[9] paper, stated that 24 cases of this condition were diagnosed in fifteen years at the St. Louis Children's Hospital. Twenty-three of these patients were operated on and 6 recovered, a rate of recovery approximating Ladd's. In the section in Christopher's "Textbook of Surgery" dealing with congenital intestinal obstruction, Ladd[10] stated that with improved technic figures for his results were superior to his former figures, 4 of his last 5 patients having recovered after primary anastomosis was performed and 13 of 20 patients with malrotation of the intestine having survived corrective operations.

Since 1933 other authors have published sporadic reports of congenital obstruction which was relieved by surgical measures.[11] In an excellent article dealing solely with anomalies of intestinal rotation, McIntosh and Donovan[12] reported that of 17 cases in which operation

8. Webb, C. H., and Wangensteen, O. H.: Congenital Intestinal Atresia, Am. J. Dis. Child. **41**:262 (Feb.) 1931.

9. Ladd, W. E.: Congenital Obstruction of the Small Intestine, J. A. M. A. **101**:1453 (Nov. 4) 1933.

10. Ladd, W. E.: Anomalies of the Small Intestine, in Christopher, F.: Textbook of Surgery, Philadelphia, W. B. Saunders Company, 1936, p. 1175.

11. (*a*) Carter, R. F.: Congenital Occlusion of Duodenum and Small Intestine: Clinical Considerations and Report of Two Cases, J. Pediat. **2**:27, 1933. (*b*) Davenport, G. L., and Goldberg, S. L.: Obstruction from Fetal Peritonitis in Premature Infant: Operation and Recovery, Illinois M. J. **66**:563, 1934. (*c*) Donovan, E. J.: Congenital Atresia of the Duodenum in the Newborn, Ann. Surg. **103**: 455, 1936. (*d*) Martin, J. D., and Elkins, D. C.: Congenital Atresia of the Intestine, ibid. **105**:192, 1937. (*e*) Jones, T. B., and Morton, J. J.: Congenital Malformation of the Intestine, Am. J. Surg. **39**:382, 1938. (*f*) Stenson, W.: Duodenal Occlusion in Newborn: Successful Operation on Premature Twin, Am. J. Dis. Child. **56**:1066 (Nov.) 1938. (*g*) Cathcart, D. F.: Congenital Intestinal Anomaly in a Newborn Infant, ibid. **55**:566 (March) 1938.

12. McIntosh, R., and Donovan, E. J.: Disturbances of Rotation of the Intestinal Tract, Am. J. Dis. Child. **57**:116 (Jan.) 1939.

was performed, cures resulted in 8. Gardner and Hart [13] analyzed 32 cases of volvulus neonatorum, in 16 of which operations were performed, with 8 recoveries (50 per cent). The changing view of the prognosis of this disorder is reflected in the progressive editions of Holt and Howland's book, "Diseases of Infancy and Childhood." Thus, in the seventh edition (1917) the authors stated that the prognosis was almost invariably fatal, while in the tenth edition, edited by L. E. Holt Jr. and R. McIntosh in 1933,[14] it was stated that an appreciable number of patients had been successfully operated on in recent years. Montgomery,[15] in his article on this subject in Brennemann's textbook of pediatrics, recommended operation once the diagnosis is made. On the other hand, Griffith and Mitchell [16] and Kleinschmidt,[17] in Pfaundler and Schlossmann's "Diseases of Children," have not yet expressed this alteration in the prognosis.

Since 1931, when Webb and Wangensteen [8] reported that they had found mention of more than 500 cases of intestinal atresia in the literature, at least 150 additional cases have been recorded. Up to 1931 only 9 survivals had been reported. More than 50 cases have been recorded in which the patient responded to surgical measures. It should be remembered that in many cases reported no surgical intervention was attempted. For instance, at the Great Ormond Street Hospital of London, 29 autopsies were performed in cases of intestinal atresia from 1900 to 1929, but not a single operation was attempted.[11d] Today the chance of success from an operation performed by skilled hands may be calculated, according to several sources,[18] as about 25 per cent. It is to be hoped that this figure will be further bettered with the establishment of earlier diagnosis, with less delay in performing the operation and with the perfecting of technic. By the application of newer methods of intravenous therapy for babies, which permit a much longer rest of the intestine, postoperative treatment has been tremendously improved

13. Gardner, C. E., Jr., and Hart, D.: Anomalies of Intestinal Rotation as a Cause of Intestinal Obstruction, Arch. Surg. **29**:942 (Dec.) 1934.

14. Holt, L. E., and Howland, J.: Diseases of Infancy and Childhood, revised by L. E. Holt Jr. and R. McIntosh, ed. 10, New York, D. Appleton-Century Company, Inc., 1933, p. 294.

15. Montgomery, A. H.: Diseases of the Small Intestine, Cecum, Peritoneum and Omentum, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1937, vol. 3, chap. 6.

16. Griffith, J. C., and Mitchell, A. G.: Diseases of Infancy and Childhood, Philadelphia, W. B. Saunders Company, 1937, pp. 593-594.

17. Kleinschmidt, H.: Diseases of the Stomach and Intestines, in von Pfaundler, M., and Schlossmann, A.: Diseases of Children, translated by M. B. Peterman and others, Philadelphia, J. B. Lippincott Company, 1935, vol. 4, p. 210.

18. Ladd (footnotes 9 and 10). Carter.[11a]

because of the better maintenance of water and electrolyte balance, which former methods of parenteral therapy did not permit.[19]

Webb and Wangensteen [8] stated that in their experience the incidence of intestinal atresia is 1 case to each 4,000 infants born. Some authorities have reported a lower incidence.[20] At the Jewish Maternity Hospital, in the last three years, I have noted 6 cases of congenital intestinal obstruction among the 6,000 babies born. When it is considered that the United States Public Health Service has reported the births of 2,000,000 babies annually in the United States, it becomes evident that this is not an excessively rare disease, for hundreds of babies in this country must die each year from this condition.

Birgfeld,[21] in 194 cases, found the distribution of the obstruction to be as follows:

	Number	Percentage
Duodenum	58	30
Small intestine	103	53
Colon	33	17

These figures are in accord with the lower incidence of duodenal atresia reported in the literature. However, Cole,[9] in commenting on 24 cases of congenital intestinal obstruction, stated that in 13 the atresia was in the duodenum; in 11, in the ileum. The site of the atresia in Webb and Wangensteen's [8] 17 cases was: duodenum, 7 cases, in 2 of which it was above and in 5 below the papilla of Vater; ileum, 7 cases; jejunum, 2 cases, and colon, 1 case. Of the 6 patients I have recently encountered, obstruction has been in the duodenum in 5.[21a]

The question of multiple atresias always arises when operation for congenital atresia of the intestine is advised. Davis and Poynter [20] gave statistics showing that only in 15 per cent of patients with congenital intestinal obstruction are there multiple atresias. Richter [5] put the figure for the incidence of multiple atresias as high as 25 per cent. It has been my experience that multiple lesions are more common in patients with atresia of the ileum and colon and rare in those with atresia of the duodenum. In cases of anomalies of intestinal rotation more than one

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19. Standard, S.: Water and Salt Metabolism, Internat. Abstr. Surg. **67**:301, 1938; in Surg., Gynec. & Obst., October 1938. Coller, F. A.; Bartlett, R. M.; Bingham, D. L. C.; Maddock, W. C., and Pedersen, S.: The Replacement of Sodium Chloride in Surgical Patients, Am. J. Surg. **108**:769, 1938.

20. Davis, D. L., and Poynter, C. W. M.: Congenital Occlusion of the Intestine with Report of Multiple Atresia of the Jejunum, Surg., Gynec. & Obst. **34**:35, 1922.

21. Birgfeld, E.: Zur kongenitalen Dünndarmatresie, Zentralbl. f. Chir. **55**: 1548, 1928.

21a. Since this paper was submitted for publication I have seen 2 additional patients with congenital obstruction of the ileum.

intestinal anomaly is commonly found, but such conditions are often amenable to surgical treatment.[22] These facts and figures, instead of deterring, should encourage the surgeon to operate.

Not infrequently abnormalities of other parts of the body are also present. Of these, mongolism has been the most common, a fact commented on by other authors.[11e] Polyhydramnios in the mother has often been a harbinger of congenital anomalies in the baby (in such sites as the intestine and brain).[23] Other abnormalities of the intestinal tract should be searched for at operation, such as malrotation of the intestine and stomach, defects and deviation of the mesentery, anomalous course of blood vessels and congenital bands.[24] If at operation no such anomalies are seen and no atresia is visible but unquestioned signs of intestinal obstruction are observed, a diaphragm should be searched for at the site of the obstruction, as in 1 of my patients (case 1); instances of such a condition have been reported in the literature.[25] The familial incidence of intestinal atresia and related anomalies has been commented on by some writers.[26]

A diagnosis of congenital intestinal obstruction is not difficult if one bears this condition in mind when examining every patient with persistent vomiting from birth. Curiously enough, this vomiting is often not projectile and seldom has the expulsive force of the vomiting of patients with pyloric stenosis. When the obstruction is above the papilla of Vater there is no bile in the vomitus. The diagnosis is then more difficult, but this condition can be differentiated from pyloric stenosis by the earlier onset and by roentgen studies and a scrupulous examination of the meconium. It may here be said that pediatricians are too apt to scan the meconium on the diaper with skilful neglect. When the obstruction is above the papilla of Vater the meconium may seem normal, but examination according to the technic of Farber [27] will show the absence of keratinized epithelium, for the swallowed amniotic fluid does not become part of the meconium because of the obstruction. When the obstruction is below the papilla of Vater the vomitus may be a brilliant shamrock green or an ominous golden yellow, which should suggest the

22. McIntosh and Donovan.[12] Gardner and Hart.[13]

23. Weeks and Delprat.[7d] Webb and Wangensteen.[8]

24. McIntosh and Donovan.[12] Gardner and Hart.[13] Davis and Poynter.[20]

25. Garvin, J. A.: Congenital Occlusion of the Duodenum by a Complete Diaphragm, Am. J. Dis. Child. **35**:109 (Jan.) 1928. Krieg, E. G.: Duodenal Diaphragm, Ann. Surg. **106**:33, 1937. Ladd (footnotes 9 and 10).

26. (*a*) Farr, C. E., and Fries, M. E.: Congenital Occlusion of the Bowel, S. Clin. North America **5**:621, 1925. (*b*) Denny, E. S., and Sloan, L. H.: Congenital Intestinal Malformation in Identical Twins, ibid. **12**:227, 1932. Rogers.[2]

27. Farber, S.: Congenital Atresia of the Intestine: Diagnosis by Microscopic Examination of the Meconium, J. A. M. A. **100**:1733 (June 3) 1933.

diagnosis, because bile is conspicuously absent from the vomitus of patients with pyloric stenosis.[28] The meconium, lacking amniotic fluid and bile, is scant and does not have its characteristic dark color, but resembles grayish green viscid mucus. It is relatively devoid of keratinized epithelium and lanugo.[27] On examination, the stomach is generally found to be markedly dilated, and in patients with duodenal obstruction a huge duodenum can often be seen and felt in the right upper abdominal quadrant. This should not be confused with a pyloric tumor, for the ballooned duodenum is large, soft and gurgling and seems more superficial. Visible gastric peristalsis may or may not be observed in patients with high intestinal obstruction; intestinal peristalsis may be observed in patients with low intestinal obstruction. The gastric and duodenal regions may be much distended in patients with atresia of the duodenum, and the whole upper part of the abdomen, or even most of the abdomen, may be distended when there is an obstruction in the ileum or colon. Signs of general dehydration ensue if the disease is allowed to run its course without relief of the obstruction.

I have found the plain roentgenogram without the use of a contrast medium invaluable in confirming the clinical diagnosis, for several reasons. First, it is a simple and harmless method, and the dangers attending the use of barium are avoided.[29] Second, it is time saving. Third, the lesions are clearly shown, and the site of the obstruction in patients with atresia or stenosis is as well outlined as with the use of the barium paste (compare *A* and *B* of figure 3 and *B* and *C* of figure 4). Fourth, it is objective and helps to convince a skeptical surgeon, who may be inclined to doubt a purely clinical diagnosis and advise watchful waiting until the diagnosis is established with certainty.

In the literature there is a paucity of illustrations and descriptions of roentgenograms of the abdomen of newborn children taken without barium, the so-called plain roentgenogram. Accordingly, in order to evaluate properly such films, in which spontaneously swallowed air is the contrast medium, normal babies were examined at different intervals after birth. According to Golden[30] and Snow,[31] gas is normally present in the small intestine of an infant, but they did not give illustrations or such details as how long the gas is present and the age of the infant. A roentgenogram of a baby's abdomen made before

28. Donovan, E. J.: Congenital Hypertrophic Stenosis, Am. J. Surg. **39**:377, 1938.

29. Webb and Wangensteen.[8] Ladd (footnotes 9 and 10). Montgomery.[15]

30. Golden, R.: Diagnostic Roentgenology, New York, Thomas Nelson & Sons, 1936, p. 302.

31. Snow, W.: Postural Treatment of Infantile Colic, Am. J. Roentgenol. **38**:779, 1937. Snow, W., and Cassasa, C. S.: Postural Treatment of Tympanites, J. A. M. A. **104**:1403 (April 20) 1935.

it has taken anything by mouth shows a generous amount of gas in the stomach and in the intestine (fig. 1 *A*). This can reasonably be interpreted as due to the amniotic fluid swallowed by the baby during the process of delivery. If there is an obstruction, the swallowed air will not assist in visualization beyond the site of the obstruction but will clearly outline the dilated stomach, the duodenum or the coils of the intestine proximal to the obstruction.

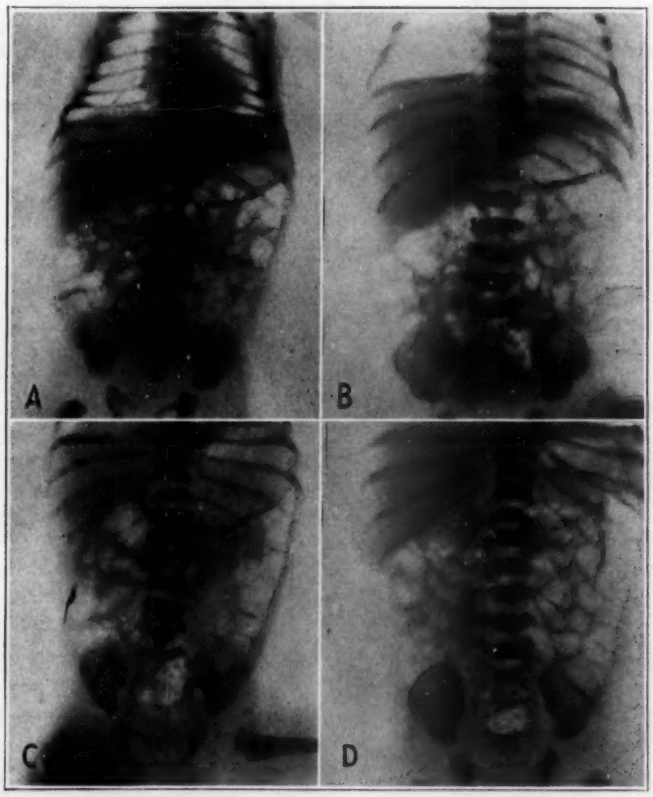

Fig. 1.—Abdominal roentgenograms of normal children made without using a contrast medium. *A*, taken three hours after birth. Note air in the stomach and intestines, which, since the baby had taken nothing by mouth, must have been swallowed during birth. *B*, taken at 2 days of age. The swallowed air outlines all parts of the gastrointestinal tract. *C*, taken at 3 days of age. The stomach, small intestine and colon are all clearly outlined. *D*, taken at 5 days of age. This picture is essentially the same as *C*, and the same is true of pictures taken at later intervals.

Pyloric stenosis is always the first diagnosis to come to the mind of the surgeon not familiar with the duodenal obstruction of the newborn. Roentgenograms of the abdomen of babies with pyloric stenosis made

without using a contrast medium have shown a stomach which is large, but not nearly as large as the dilated stomach due to duodenal atresia or stenosis (figs. 2, 3 *A*, 5). This is an important differential point.[28] Of course, there is no dilated duodenum in patients with pyloric stenosis. Furthermore, there is free passage of the swallowed air through the entire intestinal tract of patients with pyloric stenosis. A knowledge of such findings is of great value in interpreting the roentgenogram of the newborn baby made without using a contrast medium.

It is to suggest a wider use of this simple method in the diagnosis of congenital obstruction that I report cases in which such films clinched

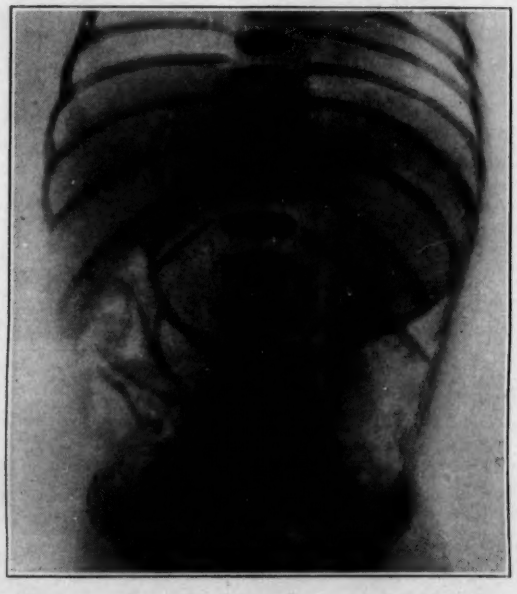

Fig. 2.—Roentgenogram, made without using a contrast medium, of the abdomen of a patient with pyloric stenosis (proved by operation). The dilated stomach is clearly outlined, and the presence of air in the small intestine and colon is clearly indicated.

the diagnosis and hastened operation. In 1 the result was successful. The simple abdominal roentgenogram is by no means new. It has been suggested by several authors,[32] but there is little or no mention of it in textbooks of pediatrics[33] or pediatric systems.[34] I believe that this method should be used routinely in examining newborn infants suspected of having intestinal obstruction. Comparative studies have shown that

32. Ladd (footnotes 9 and 10). Martin and Elkins.[11d] Jones and Morton.[11e]

33. Footnote 1. Holt and Howland.[14] Griffith and Mitchell.[16]

34. Richter.[5] Montgomery.[15] Kleinschmidt.[17]

the obstructive lesions are indicated as well by the spontaneously swallowed air as by barium (figs. 3 *A*, 3 *B*, 4 *B*, 4 *C*). Internists and surgeons regularly invoke the aid of simple abdominal roentgenograms in cases of acquired intestinal obstruction, but this method is not sufficiently used by pediatricians when working with newborn babies.[35] It is routinely applied at the Beth Israel Hospital.

REPORT OF CASES

CASE 1.—L., a girl, was born Sept. 11, 1938. There had been polyhydramnios in this and in her mother's previous pregnancy, which had resulted in a child with a cerebral defect. The patient, who was born prematurely (at the eighth month) was cyanotic at birth. She had aspirated a large amount of mucus, which had to be suctioned out. Since birth there had been nonprojectile vomiting of a turbid milky fluid which contained no bile. No meconium was passed for two days, and rectal irrigation resulted in a clear return of fluid. On the third day of life, a catheter was passed into the stomach, which seemed huge, and cloudy fluid containing minute brown particles was aspirated. Analysis of the gastric contents showed no free acid, a total acidity of 15 and small amounts of steapsin (0.2 units).

Physical examination revealed a small premature baby, 2 days old, who weighed 5 pounds (2,268 Gm.) and exhibited features of mongolism. The stomach was markedly dilated, and no visible peristalsis was noted. A diagnosis of obstruction in the first part of the duodenum was made because of: (1) vomiting, of regurgitation type, since birth; (2) passage of no stools and little meconium; (3) marked dilatation of the stomach without a palpable tumor, and (4) absence of bile from the vomitus.

A simple roentgenogram of the abdomen showed a markedly dilated stomach and no evidence of gas beyond the pylorus or the first part of the duodenum (fig. 3 *A*). This confirmed the diagnosis of obstruction of either the pylorus or the adjacent portion of the duodenum. The roentgenogram with barium as a contrast medium showed no pyloric evacuation, indicating complete obstruction at the pyloroduodenal junction.

Operation.—Preliminary transfusion was given and continuous intravenous therapy was instituted. At operation, performed September 16, when the patient was 5 days old, the stomach was markedly dilated, but the duodenum appeared normal. No external cause for obstruction was evident; there was no condition such as bands, intestinal malrotation or atresia. The distal portion of the stomach was compressed, and no gas passed into the duodenum.

An incision was made horizontally into the duodenum, just beyond the pylorus. A probe passed into the duodenum met no obstruction. The probe was then passed through the duodenal opening of the pylorus and encountered a complete septum at the pylorus. Under the pressure, a membrane ballooned out from the stomach into the duodenal opening. This membrane, which was causing complete obstruction, was incised; the distended stomach collapsed, and a little secretion and barium came through. The membrane was incised in all directions, and a Heineke-Mikulicz type of pyloroplasty was performed, the transverse wound being sutured in a vertical direction.

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35. Solis-Cohen, L., and Levine, S.: X-Ray Diagnosis of Complete and Partial Intestinal Obstruction, Radiology **31**:8, 1938. Ginzburg, L.: X-Ray Diagnosis of Acute Intestinal Obstruction Without Use of Contrast Media, Ann. Surg. **96**:368 (Sept.) 1932.

Course.—On September 19 the baby passed normal stools; she still vomited at times, but the vomitus now contained bile. Feeding was resumed six hours after the operation, but the continuous intravenous treatment and transfusion were continued, as only 2 ounces (59 cc.) of milk was given the first day. Physiologic jaundice had disappeared and the weight was 5½ pounds (2,495 Gm.). By September 23 the baby was consuming a formula containing 23 calories per pound of body weight. By October 2 she was eating well, with no vomiting, and passing good stools; her weight was stationary.

On October 4 her temperature, previously normal, rose to 100.4 F. Vomiting, of nonprojectile type, occurred at frequent intervals, the material containing bile but no blood; the stools were normal. On October 5, nineteen days after the operation, her temperature rose to 106.2 F. Feeding by mouth was discontinued and transfusions and continuous intravenous therapy were again instituted. On October 7 her temperature was 100.5 F. and the intravenous drip apparatus became clogged and its use had to be discontinued. The child was dehydrated. A solution of dextrose was given by mouth and subcutaneously.

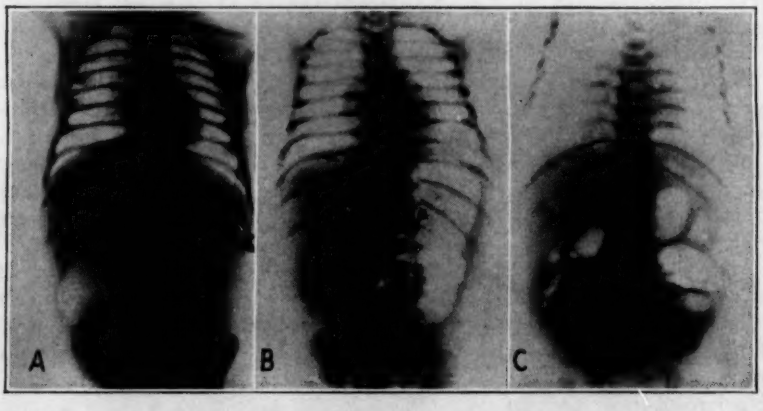

Fig. 3 (case 1).—Abdominal roentgenograms of a baby who had a septum at the pyloroduodenal junction. *A*, taken at 4 days of age without using a contrast medium, showing the large dilated duodenum, with complete obstruction which prevented the swallowed air from passing beyond this point. *B*, taken at the same time as *A* but with barium as a contrast medium. Note that the lesion is not better revealed by using barium, which had not passed beyond the duodenum at the end of four hours. *C*, taken twenty-three days later, after operation, showing obstruction in the small intestine.

On October 8 the abdomen was diffusely distended. There had been no bowel movement for forty-eight hours. The presence of an intraperitoneal inflammatory process, with secondary obstruction, was now suspected. This suspicion was verified by a roentgenogram of the abdomen, taken without using a contrast medium (fig. 3 *C*). Study of these films seemed to indicate the presence of an obstruction in the jejunum, since the stomach was dilated and several loops of small bowel could be seen. The roentgenologist reported that there was a mechanical obstruction in the upper part of the small intestine. There had been no bowel movement for three days. Gastric lavage was performed.

On October 10 a transfusion was given, and continuous intravenous therapy was once more begun. The child was examined, and an operation to relieve the secondary obstruction was about to be performed when she passed a stool; so the operation was deferred.

On October 11 the temperature was normal, there was no vomiting and stools were passed. A flat plate of the abdomen showed gas traversing the intestine normally. The abdomen was still distended, but not as much as before.

By October 14 the intra-abdominal inflammation and the intestinal obstruction were subsiding spontaneously. There was now an infection of the respiratory tract, with some fever. The heart and lungs were normal, and examination of the urine gave negative results.

On October 15 a blood culture was reported as negative. The child had been well for five days; the bowels were normal, and there was no vomiting. The rest of the course was uneventful, and the child was discharged from the hospital in good condition on October 26, weighing 6 pounds 3 ounces (2,807 Gm.). To date the child, although she is a mongolian idiot, has kept well, with normal gastrointestinal function and good nutrition.

Summary.—The striking features of this case were: (1) Both the patient and the child resulting from the mother's previous pregnancy were abnormal; (2) both pregnancies were characterized by polyhydramnios; (3) early diagnosis was made with the aid of abdominal roentgenograms; (4) early operation with incision of a pyloroduodenal septum was performed, and (5) water and electrolyte balances were maintained in the patient by continuous venoclysis, to the point of edema. The baby for six weeks took little food by mouth.

CASE 2.—M., a girl, was born Sept. 26, 1938, at full term of a primipara. When first seen she was 3 days of age and had typical signs of mongolism. The chief complaint was the vomiting of yellow fluid since birth. Nothing but meconium had been passed for three days. Examination showed the outline of a huge stomach, with visible peristalsis and a palpable tumor in the right paraumbilical region. This impressed me as being not a pyloric tumor but rather a dilated duodenum. A simple roentgen examination of the abdomen (fig. 4 *A*) showed there was a collection of gas in the upper left quadrant and in the proximal duodenal loop, findings suggesting duodenal stenosis.

Course.—The child was dehydrated; so parenteral therapy was instituted. The hemoglobin content was 144 per cent. There were 8,000,000 red cells and 5,000 white cells per cubic millimeter, with 51 per cent lymphocytes, 47 per cent polymorphonuclears and 2 per cent neutrophilic stab forms.

Owing to the fact that the child was a mongolian idiot, the parents refused to consent to an operation, and the matter was not pressed.

On October 5 the child, now 9 days of age, passed her first stool since birth. It consisted of 15 cc. of dark brown, thick meconium. She had been vomiting everything since birth; the weight had been kept constant with the aid of parenteral therapy. Examination of the meconium showed a positive benzidine reaction for blood (4 plus); red blood cells and epithelial cells were discovered by Farber's method.[27] The next day the baby vomited less frequently. On October 8 the child was still vomiting fluid containing bile, the abdomen was distended and peristalsis was still visible. Parenteral therapy was still being continued.

On October 10 a real stool was passed, which contained blood and bile. Roentgenograms, which were made with and without the use of barium, showed a small amount of barium in the duodenum, at the end of which there was an obstruction.

At 17 days of age bronchopneumonia developed and the patient died.

Autopsy.—The anatomic diagnoses were: mongolism; severe stenosis of the duodenojejunal junction, with marked dilatation of the proximal portion of the duodenum and the stomach; bronchopneumonia, with emphysema and atelectasis, and anomalous origin of the right subclavian artery.

The distention of the stomach was marked; the pyloric lumen was quite adequate; the entire duodenum was markedly distended, and its walls were almost paper thin. At the most distal portion of the retroperitoneal segment, the duodenum came to an almost blind ending. Careful probing revealed an opening less than 1 mm. in diameter between the duodenum and the jejunum.

Interstitial pancreatitis, with numerous polynuclear and mononuclear cells, was probably secondary to the duodenal stenosis, a dilatation with damming back along the pancreatic ducts.

Summary.—The notable features of this case were: (1) The patient had mongolism; (2) the condition was diagnosed as stenosis and not as atresia because

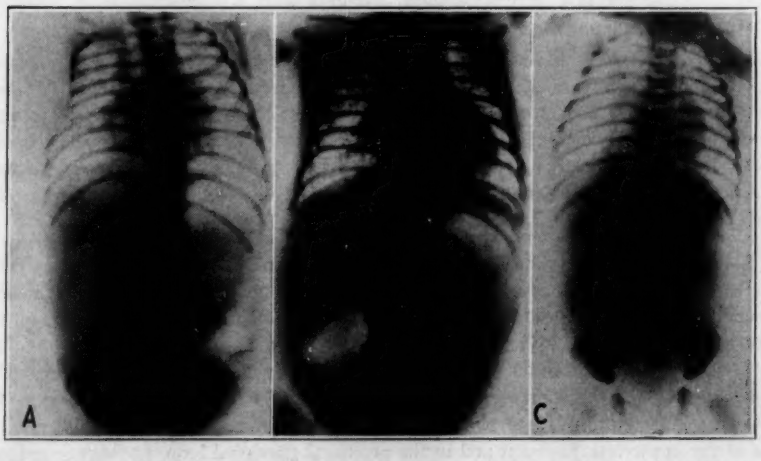

Fig. 4 (case 2).—Abdominal roentgenograms of a baby who had stenosis, with a pinpoint opening, at the duodenojejunal junction. *A*, taken at 4 days of age without using a contrast medium, showing the stomach and duodenum filled with air, which does not pass beyond the duodenum. *B*, taken at 17 days of age, showing obstruction at the end of the duodenum, which seems coiled on itself in this picture. *C*, taken at the same time as *B* but with the use of barium. There was no advantage in using barium as a contrast medium.

of finding keratinized epithelium by Farber's method; (3) the diagnosis was established by means of a roentgenogram made without using a contrast medium; (4) interstitial pancreatitis was present, and (5) no operation was performed, death being due to aspiration pneumonia.

CASE 3.—Y., a boy, was born Sept. 30, 1939, supposedly at full term, of a primipara. Since birth, the child had vomited bilious material. When seen on the second day of life the baby weighed 4 pounds 4 ounces, looked immature and had green stains (bile) on the front of his nightshirt. The stomach was huge; no visible peristalsis was observed. In the right hypochondrium a soft, superficial, gurgling mass, the size of a golf ball, was palpable, which, because of its character,

I believed was the dilated duodenum. Meconium had been passed, but none had been saved, and no detailed observations were made. A diagnosis of duodenal atresia below the papilla of Vater was made and immediate operation advised. Roentgenograms, without use of barium, showed marked distention of the stomach and the first portion of the duodenum, due to atresia of the duodenum (fig. 5). At operation, a huge malrotated stomach was seen, with a dilated duodenum surrounded by pancreatic tissue. Atresia was found just below the papilla of Vater. The pylorus was directed posteriorly and fixed to the midline, with rotation of the stomach. The pylorus was continuous with the duodenum, which in the second portion became conical and ended blindly below the papilla of Vater. In spite of such measures as transfusions and intravenous therapy, the child died the next day. The cause of death, as revealed by autopsy, was hemoperitoneum.

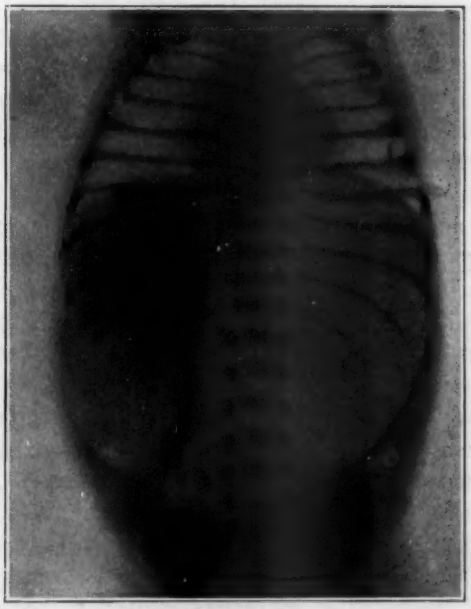

Fig. 5 (case 3).—Abdominal roentgenogram of a baby 1½ days old, showing enormously dilated stomach and duodenum, with complete obstruction, as air did not pass beyond the duodenum. At operation duodenal stenosis below the papilla of Vater was disclosed.

Notable features of this case were:

(1) The diagnosis was made by means of a roentgenogram; (2) the dilated duodenum was palpable, and (3) operation was performed when the patient was 44 hours of age.

COMMENT

The familial incidence of congenital intestinal malformation has been commented on by several authors.[36] The mother of 1 patient in my

36. Rogers.[2] Farr and Fries.[26a] Denny and Sloan.[26b]

small series had a sister with a baby who suffered from intestinal obstruction at birth. A sibling of another patient died of cystic pancreatic disease, with changes in the ducts. A sibling of another patient also died of some cerebral degenerative disease. It is important to bear the familial incidence in mind, as the question is often asked, "Will the next baby have a similar or allied disease?"

In a baby born with obstruction of some part of the gastrointestinal tract there are often other anomalies. These may be in the intestine or in other parts of the body. Two of my patients had mongolism, an occurrence previously noted in the literature.[11e] One patient at autopsy was found to have interstitial pancreatitis, which may have been due to damming up behind the duodenal atresia situated below the papilla of Vater, or perhaps to associated anomalies of the pancreatic ducts. The course of the left subclavian artery of this child also was anomalous. One of my patients with duodenojejunal stenosis had associated malrotation of the intestine and obstruction of the ileum, which was trapped behind a mesentery that pursued an anomalous course. In another patient with malrotation of the intestine the jejunum was trapped behind the mesentery, and the duodenum was obstructed by the anomalous course of the superior mesenteric artery. Anomalies such as these have been well described in the literature,[37] and it behooves the surgeon operating for relief of intestinal obstruction to be thoroughly familiar with malrotation of the intestine and the associated aberrant course of the mesentery, or the operation will be incomplete. In some patients there may be two or more types of obstruction, with the consequence that if only one is corrected at operation the patient will still die of intestinal obstruction. This happened in 2 of my cases. If a surgeon, bearing these facts in mind, is trained to perform these operations the results will be much better. This is apparent in certain reports on this subject.[38] Four of my patients were operated on, and 1 recovered.

The medical treatment is extremely important, because before the operation and for some time after the baby is dehydrated and in a state of virtual starvation. The treatment that I follow is the same as that used to relieve the alimentary intoxication of dehydrated infants.[39] Continuous intravenous therapy, with frequent transfusions, is the routine

37. Dott, N. M.: Volvulus Neonatorum, Brit. M. J. **1**:230, 1927. McIntosh and Donovan.[12] Gardner and Hart.[13]

38. Webb and Wangensteen.[8] Ladd (footnotes 9 and 10). McIntosh and Donovan.[12]

39. Karelitz, S.: The Continuous Intravenous Method of Fluid Administration (Venoclysis) in Pediatrics, New York State J. Med. **34**:631, 1934. Karelitz, S., and Schick, B.: Treatment of Toxicosis with Aid of Continuous Intravenous Drip of Glucose, Am. J. Dis. Child. **42**:781 (Oct., pt. 1) 1931; Treatment of Alimentary Toxicosis, J. A. M. A. **99**:366 (July 30) 1932.

followed. On the second day after the operation, small amounts of a dilute milk formula are given at frequent intervals, with a gradual increase in the amounts until the caloric intake is adequate. During this period, the requirements of fluid and salt are guaranteed by infusion. Since in these tiny babies the needles are apt to become clogged if this treatment is continued for days, somewhat more than absolutely necessary amounts of isotonic solution are frequently given. On several occasions this has resulted in edema which, when the needle became clogged and the infusion was discontinued, proved to be welcome reservoirs of water and salt for the next few days. If necessary, after these were exhausted another infusion was instituted.

SUMMARY AND CONCLUSIONS

In view of the greatly improved prognosis for congenital intestinal obstruction if operation is performed, it is important to arrive at a speedy diagnosis.

The roentgenogram made without using a contrast medium, by virtue of its objectivity, has been invaluable in verifying the suspicion of congenital obstruction based on clinical observations.

Of 4 of my patients with congenital intestinal obstruction who were operated on, 1 survived.

Roentgenograms of the gastrointestinal tracts of normal babies were made without using any contrast medium but the air which had been spontaneously swallowed. The course and distribution of this air along the gastrointestinal tract in such roentgenograms taken at different intervals after birth are illustrated and described. These roentgenograms look far different from those taken of the intestinal tracts of babies with intestinal obstruction, in which the column of air is cut off at the site of obstruction, with dilatation of the portions of the gastrointestinal tract proximal to the obstruction.

1175 Park Avenue.

News and Comment

GENERAL NEWS

The American Board of Pediatrics.—An examination will be held in Boston on October 12, 1941, immediately following the meeting of the American Academy of Pediatrics.

No further applications for the examination to be held in New York, in March 1941, can be accepted because the list is now closed.

The following physicians have been certified by the American Board of Pediatrics since the last report:

M. Vaun Adams, Mobile, Ala.; Helen Margaret Aff, St. Louis; Charles B. Alexander, San Antonio, Texas; Jennie K. Amtman, Chicago; Claude W. Ashley, Bloomsburg, Pa.; Donn J. Barber, Greeley, Colo.; Dessie M. Beach, Opelika, Ala.; Montgomery Blair Jr., Washington, D. C.; Russell C. Bond, Wheeling, W. Va.; Joseph R. Bowman, Johnson City, Tenn.; Barnett P. Briggs, Little Rock, Ark.; Ogden C. Bruton, Nashville, Tenn.; William F. Burdick, Washington, D. C.; Mario S. Cioffari, Yonkers, N. Y.; Jean D. Craven, Lexington, N. C.; Hester Balch Curtis, Santa Fe, N. Mex.; Rollin E. Cutts, Springfield, Ill.; David B. Davis, Los Angeles; Thomas J. Donovan, Houston, Texas; John E. Dunlap, Dallas, Texas; Hertha Ehlers, Los Angeles; Harold J. Eisenberg, Brooklyn; Gladys J. Fashena, Dallas, Texas; Joseph H. Fries, Brooklyn; Alice Harrison Fuller, Minneapolis; Eugene Gettelman, Chicago; Frank X. Giustra, Brooklyn; Gene B. Haber, Philadelphia; Robert B. Hightower, Washington, D. C.; Thomas Field Humphrey, Dayton, Ohio; Alton Miller Johnson, Valdosta, Ga.; George Dean Johnson, Spartanburg, S. C.; Albert Mitchell Jones, Memphis, Tenn.; Benjamin Kaufman, Brooklyn; George Francis Kelly, Milwaukee; W. Price Killingsworth, Port Arthur, Texas; I. Russel Kuhn, Brooklyn; Meyer Kurzner, Oklahoma City; Kenneth S. Landauer, Geneva, N. Y.; John T. Leslie, Griffin, Ga.; Philip Magrish, San Antonio, Texas; Mary Margaret McLeod, Trion, Ga.; Franklin J. Mellencamp, Milwaukee; Ludo von Meysenbug, Daytona Beach, Fla.; Halcuit Moore, Dallas, Texas; Ramsay Moore, Dallas, Texas; Robert Leslie Moore, Dallas, Texas; Paul Newton Morrow, Omaha; Robert Taylor Moulton, Salem, Mass.; Adolph R. Nachman, Chicago; John M. Nelson, Denver; Floyd A. Norman, Dallas, Texas; Owen S. Ogden, Louisville, Ky.; H. E. Petersen, St. Joseph, Mo.; Karin A. Petri, Houston, Texas; David C. Pewterbaugh, Chambersburg, Pa.; Rosa Elizabeth Prigosen, Brooklyn; Paul H. Rhodes, Denver; Carroll E. Roach, Greenville, Miss.; Irving Rosenbaum Jr., Louisville, Ky.; Andrew D. Shapiro, Roanoke, Va.; Samuel Shwartz, Washington, D. C.; Harold J. Starr, Chattanooga, Tenn.; Albert F. Stein, Chicago; Charles L. Steinberg, St. Paul; Joe M. Strayhorn, Nashville, Tenn.; Van C. Temple, Hattiesburg, Miss.; Edward J. Thalheimer, Vineland, N. J.; Willis H. Thompson, Nashville, Tenn.; Harry Ewing Wachter, St. Louis; John A. Washington, New York; Clarence M. Weidenthal, Cleveland; M. L. Weimann, Haddon Heights, N. J.; Vida B. Wentz, Chicago; Leta J. White, Petersburg, Va.; William Richard Whitley, Evanston, Ill.; Sherl J. Winter, Dayton, Ohio, and Martin Zeisler, Chicago.

Effect of Military Service on Candidacy for Examination of the American Board of Pediatrics.—At the annual meeting of the American Board of Pediatrics, held in Memphis, Tenn., on Nov. 16 and 17, 1940, the following action was taken in regard to service in the army or navy:

Candidates for examination by this board may substitute one year of military service for one of the required two years of pediatric practice and/or continued study. Military service cannot be substituted for any of the required preliminary hospital training, but this preliminary training may be completed after return from military service.

The secretary, Dr. C. Anderson Aldrich, 707 Fullerton Avenue, Chicago, will be glad to answer any specific questions in regard to this ruling.

SOCIETY NEWS

American Orthopsychiatric Association.—The eighteenth annual meeting of the American Orthopsychiatric Association, an organization for the study and treatment of behavior and its disorders, will be held at the Hotel Pennsylvania, New York, on Feb. 20, 21 and 22, 1941. A registration fee will be charged non-members. A preliminary program will be sent on request. Headquarters of the association are at 1790 Broadway, New York.

PERSONAL NEWS

Dr. Béla Schick Honored.—Dr. Béla Schick will be presented with a gold medal in recognition of "distinguished and outstanding contributions in the field of allergy" at the third annual forum reviewing progress in the chemical study of allergy, which will be held at Indianapolis on January 11 and 12.

Abstracts from Current Literature

Biochemistry; Bacteriology and Pathology

DROPLET INFECTION OF AIR: HIGH-SPEED PHOTOGRAPHY OF DROPLET PRODUCTION BY SNEEZING. M. W. JENNISON and H. E. EDGERTON, Proc. Soc. Exper. Biol. & Med. **43**:455 (March) 1940.

Stroboscopic illumination of high speed photography has been used to study the size and velocity of droplets given off in coughing and sneezing. In the photograph of a man at the downstroke of a sneeze as presented in the paper, 4,600 particles were counted as within the focal range of the camera. Calculations of the fastest of these droplets showed them to be moving at the rate of 100 feet per second. The number of droplets issuing from the nose is insignificant as compared to the number coming from the mouth. Problems concerning the rate of and distances to evaporation and the minimum droplet size are being investigated by the authors.

HANSEN, Minneapolis.

ELECTROMETRIC MICRODETERMINATION OF CHLORIDE IN WHOLE BLOOD SERUM AND URINE. J. LEHMANN, Acta pædiat. **26**:258, 1939.

By this method the chloride is titrated with silver nitrate, the end point being detected potentiometrically. Samples of only 0.2 cc. of fluid are required. An accuracy of 2 per cent is claimed for the procedure.

MCCUNE, New York.

Metabolism; Infant Feeding; Milk and Other Foods

THE INFLUENCE OF THE NITROGEN CONTENT OF THE DIET ON THE CALORIE BALANCES OF PRE-SCHOOL CHILDREN. JEAN E. HAWKS, JEANNE M. VOORHEES, MERLE M. BRAY and MARIE DYE, J. Nutrition **19**:77 (Jan.) 1940.

Two long-time balance experiments were carried out on 5 preschool children, in each of which two diets were given, the first containing 3 Gm. of protein per kilogram of body weight and the second 4 Gm. The latter diet, of increased protein, did not change the constant level of calory utilization. The change from the 3 Gm. to the 4 Gm. protein diet affected the calory balance by (1) increasing the nitrogen content of the excreta; (2) increasing from 7.3 to 12.0 per cent the average proportion of the intake calories eliminated, and (3) reducing the actual number and percentage of the intake calories available for body needs, producing at the same time, however, greater gains in weight.

FREDEEN, Kansas City, Mo.

THE SUPPLEMENTARY VALUE OF THE BANANA IN INSTITUTION DIETS: I. EFFECT ON GROWTH IN HEIGHT AND WEIGHT, OSSIFICATION OF CARPALS, AND CHANGES IN FRANZEN INDICES. LYDIA J. ROBERTS, RUTH BLAIR, GERTRUDE AUSTIN and GRACE STEININGER, J. Pediat. **15**:25 (July) 1939.

The authors summarize their study as follows: "The diet of 123 boys in an institution was supplemented with two to three bananas daily over a nine-month period and the effect on growth and other aspects of physical status observed in comparison with that of a control group in the same institution. . . .

"On every basis of comparison the experimental boys had some advantage over the controls. This is shown by the following:

"1. The experimental boys made a slightly greater mean gain in weight (0.90 pound) and height (0.15 inch) than the controls; a larger percentage of them

equalled or exceeded the gains 'expected' during the period (70 per cent vs. 44 per cent for weight, 71 per cent vs. 58 per cent for height); and their mean percentage gain during the year was significantly greater (127 for weight, 128 for height, vs. 105 for both weight and height).

"2. In ossification of the bones of the wrist the experimental boys also showed slightly greater progress. . . .

"3. The Franzen measurements showed a similar trend. The boys who had received the supplement made greater mean gains in measurements of arm girth, subcutaneous tissue, and weight, and also in the scores for these items. . . .

"These differences do not in most cases attain statistical significance, but the fact that they were made on matched groups and that they are consistent in direction lend support to the belief that the differences are real ones attributable to the supplement."

RAUH, Cincinnati.

THE ROLE OF BORON IN THE DIET OF THE RAT. ELSA ORENT-KEILES, Proc. Soc. Exper. Biol. & Med. **44**:199 (May) 1940.

The work of the author with rats indicates that boron is not essential for normal nutrition.

HANSEN, Minneapolis.

CANNED FOODS IN RELATION TO HEALTH. WILLIAM SAVAGE, Lancet **2**:991 (Nov. 4) 1939.

In nutritive qualities, canned foods compare favorably with fresh foods when allowance is made for the fact that the former are already prepared for use and the latter are subjected to any losses which may take place in domestic preparation and cooking. This fact applies qualitatively as well as quantitatively. In vitamin content the canned foods are in general not inferior. On the chemical side there is no evidence that tin or lead poisoning now ever results from the consumption of canned foods. From a study of all the data it can be stated definitely that canned foods are now considerably less likely than ordinary foods to be the source of food poisoning.

LANGMANN, New York.

CALCIUM AND PHOSPHORUS IN THE NORMAL INFANT. RAFAEL SOTO, Rev. mex. de puericult. **8**:357 (July) 1938.

The author reviews the daily calcium and phosphorus requirements and the way in which these substances are assimilated and discusses the normal and the abnormal calcium and phosphorus content of the blood.

HERRON, Oak Ridge, La.

THE NITROGEN, CALCIUM AND PHOSPHORUS METABOLISM OF A SEVEN MONTH OLD CHILD. G. BLUME-WESTERBERG, Acta pædiat. **26**:86, 1939.

Chemical procedures are described for the quantitative measurement of nitrogen, calcium and phosphorus in food, urine and stools. One example of a balance study involving these elements is adduced.

MCCUNE, New York.

INFLUENCE OF CITRIC ACID MILK ON THE PERCENTAGE OF CALCIUM AND INORGANIC PHOSPHORUS IN SERUM. S. SIWE, Acta pædiat. **26**: 460, 1939.

The initial ingestion of milk to which an unspecified amount of citric acid had been added produced 1 to 2 mg. of increase of serum calcium, lasting one to two hours. When the milk was consumed habitually this increase after the individual potations ceased to occur; hence, the ingestion of citric milk cannot be expected to produce even relative hypercalcium after continued use. The inorganic phosphorus

content of the serum was not affected by the citric acid milk. Since the parenteral injection of this acid usually causes a rise of both calcium and phosphorus owing to their mobilization from body stores, the conclusion is drawn that hypercalcemia unaccompanied with hyperphosphatemia is due to increased absorption. Experiments designed to classify the matter yielded paradoxic results; whereas the addition of 0.4 per cent of citric acid to milk resulted in the conversion of nearly all of the phosphorus to an ultrafiltrable state, the ultrafiltrable calcium was increased by only 3 per cent.

McCUNE, New York.

Vitamins; Avitaminoses

METABOLIC DISTURBANCES IN EXPERIMENTAL HUMAN VITAMIN B DEFICIENCY. K. O'SHEA ELSOM, FRANCIS D. W. LUKENS, ESTHER H. MONTGOMERY and LEON JONAS, J. Clin. Investigation **19**:153 (Jan.) 1940.

In a seemingly healthy woman 60 years of age, given a diet adequate except for the vitamin B complex, clinical manifestations of deficiency of the vitamin and metabolic changes became evident after five weeks but did not become striking until after eight weeks of the experimental dietary period. After eight weeks, thiamine, riboflavin and brewer's yeast were successively added to the diet. Edema appeared early and loss of weight late. Edema disappeared and normal weight was maintained only after administration of yeast. The following results were noted: 1. The level of blood sugar failed to return to normal within three to four hours after the ingestion of dextrose. This defect disappeared only after the administration of yeast. 2. Until after the administration of thiamine, the pyruvic acid in the blood rose and was still high four hours after the administration of dextrose, but the fasting level of pyruvic acid in the blood did not increase during the period of deficiency. The lactic acid content of the blood was elevated during the period of deficiency and returned to normal after the administration of thiamine. 3. The respiratory quotient remained unaltered. 4. The response to insulin decreased as the deficiency progressed. There was increased response to insulin following the administration of thiamine, and the subject became sensitive to insulin after riboflavin was added to the diet.

GUEST, Cincinnati.

BIOLOGICAL ASSAY OF THIAMIN WITH CHICKS. THOMAS H. JUKES and HUBERT HEITMAN JR., J. Nutrition **19**:21 (Jan.) 1940.

Jukes and Heitman described a method for the assay of thiamine with chicks, which uses a basal diet consisting principally of polished rice, fish meal and autoclaved yeast. Between 130 and 150 micrograms of thiamine hydrochloride per hundred grams of diet for prevention of polyneuritis was estimated in this study to be the thiamine requirement of the chick.

FREDEEN, Kansas City, Mo.

SOME REFLECTIONS ON TWO RECENT PUBLICATIONS ON RICKETS. J. P. McGOWAN, Edinburgh M. J. **47**:204 (March) 1940.

McGowan, who has written extensively on the chemistry of rickets, discusses the opinions expressed by E. A. Park in the latter's Harvey Lecture in the year 1938 to 1939. The views of Mellanby on the presence of a decalcifying factor, found especially in oatmeal, are also included in McGowan's "reflections." McGowan disagrees with both. He believes that halisteresis does exist and that this is due to a vital rather than a purely chemical process, perhaps involving the liberation of nascent phosphoric acid in the cells. McGowan has for years advocated the view that vitamin D acts by releasing phosphoric acid from the phospholipins.

NEFF, Kansas City, Mo.

FACTORS AFFECTING THE VITAMIN C (ASCORBIC ACID) CONTENT OF FRUITS AND VEGETABLES. K. W. ROBINSON and R. COURTICE, M. J. Australia **1**:787 (June 8) 1940.

Tests indicate that the loss of vitamin C in peas, beans, pawpaws and oranges is considerably less when these foods are refrigerated than when they are stored at room temperature. The vitamin C content of cabbage and pawpaws is greatest in the outer leaves and increases with full ripening. TENNEY, Madison, Wis.

METABOLISM OF THE RETINA IN AVITAMINOSIS. F. DE LEONIBUS, Ann. di ottal. e clin. ocul. **67**:512 (July) 1939.

The chemistry of visual purple and its derivative retinene is reviewed. In the author's experiments, albino rats were placed on a vitamin A-free diet until many showed signs of keratomalacia. The retinas were removed and placed in a Warburg respirator, the retina of a control animal being submitted to the same technic with that of each avitaminotic animal. No difference was found in oxygen consumption between the two groups of animals. The glycolytic power, however, was constantly higher in the retina of the avitaminotic animal, the average increase above normal being 8.6 per cent. S. R. GIFFORD. [ARCH. OPHTH.]

ACTION OF VITAMIN B_2 ON THE EXCRETION OF CREATINE AND CREATININE IN CHILDREN. B. VASILE and F. PECORELLA, Pediatria **47**:564 (July) 1939.

Four children from 6 to 8 years old on a diet free of creatine were later given vitamin B_2 for seven to nine days. The dose employed was 0.12 to 0.08 mg. per kilogram of body weight. The vitamin was given subcutaneously twice a day. The levels of creatine and creatinine were determined both before and after administration of the vitamin. There were rapid diminution and disappearance of the creatine in the urine. This reappeared only after use of the vitamin had been stopped for a few days. The creatinine was also diminished. This action of the vitamin is discussed by the authors as hindering the elimination of creatine.

MARTOCCIO, Utica, N. Y.

INFLUENCE OF A FIVE PER CENT SOLUTION OF DIHYDROTACHYSTEROL ON THE LENS IN TETANY. W. RAUCH, Arch. f. Ophth. **140**:334, 1939.

In 1927 Holtz discovered that irradiated ergosterol cured experimental rickets in rats. Large doses had pronounced toxic effects. The blood calcium rose at the expense of the bones, which were deprived of their calcium. Irradiated ergosterol was thus found to have a pronounced calcium-mobilizing effect, which was subsequently traced to a derivative of ergosterol of the composition dihydrotachysterol. This substance proved to be of great therapeutic value in cases of tetany (Holtz, 1933), in which it raised the blood calcium, lowered the nervous hyperexcitability and thus prevented convulsions.

The author of the paper under review has studied the effect of dihydrotachysterol on parathyroprival tetany of young rats. He has found that the substance is capable of preventing the outbreak of tetany and the development of opacities of the lens after destruction of the parathyroids by cauterization. "Just as definitely established is in certain stages of tetany cataract the regression of the lens opacities up to the point of perfect clearness of the lens." The protective effect of dihydrotachysterol outlasts by a few weeks the period of its administration. For permanent protection of the lens, the treatment must be kept up continuously.

In tetany of man the protective effect of dihydrotachysterol has been established with certainty. Whether or not tetanic lens opacities in man can be made

to disappear by the use of this substance is not known. "That dihydrotachysterol is out of the question as a form of treatment for senile cataract need not be stressed."

P. C. KRONFELD. [ARCH. OPHTH.]

INCREASING RESISTANCE BY PROPHYLACTIC MEDICATION WITH VITAMIN C. M. PETERS, Ztschr. f. Kinderh. **61**:179 (Aug. 9) 1939.

One group of infants was given ascorbic acid (1 tablet of cebione) daily, and another group was given no vitamin C. No significant difference in morbidity, course and duration of infections of the respiratory tract among the two groups was observed. Balance studies were not carried out.

SIEMSEN, Chicago.

TREATMENT OF RICKETS WITH A SINGLE MASSIVE DOSE OF VITAMIN D_2. S. GUNNARSON, Acta pædiat. **25**:69, 1939.

The prefatory remarks relate briefly the history of the development of the *Stosstherapie* of rickets from Vollmer's original experiments with rats and somewhat less successful clinical trials, through Harnapp's reintroduction of the method down to its growing acceptance in those countries where the prevalence of severe rickets still constitutes a serious problem. The doses that have been recommended vary between 250,000 and 4,000,000 U. S. P. units; those most frequently employed, between 600,000 and 1,000,000 units. The entire amount is given at one time, and the dose is not repeated unless the substance is vomited immediately. Although hypercalcemia and cardiac and renal damage have been anticipated and looked for, they have not been demonstrated to date. Healing of rickets occurs much more rapidly than with the customary daily treatment with smaller doses. The first chemical evidence of improvement in the blood may be detected at the end of forty-eight hours. The time required for the skeleton to assume an entirely normal roentgen aspect varies with the severity of the condition. Gratifying results have been obtained in cases of tetany. The method is especially recommended in the presence of pneumonia and pertussis. It opens new possibilities for prophylaxis. Intramuscular injection is also being tried.

The author reports experience with the oral administration of single doses of vitamin D_2, varying in size from 500,000 to 1,500,000 units, to 25 children with rickets of moderate to marked severity. Frequent roentgen studies and chemical studies of the blood were made in all cases and electrocardiograms in 9. The results were highly satisfactory. Craniotabes commenced to heal on the fifth day. Hyperphosphatemia was usual by the fifth day and persisted for about two weeks. Low values for calcium returned to normal; normal values were unaffected. Healing was evident on roentgen examination at the end of a week in all cases and in some at four days. No manifestations of harm were detected.

McCUNE, New York.

EARLY ROENTGEN SIGNS OF RICKETS. K. LINDBLOM, Acta pædiat. **25**:170, 1939.

Controlled roentgen investigation of 69 healthy newborn infants who were deprived of vitamin D or given it according to various schedules and of 8 infants with rickets and tetany led to the following conclusions: "The classical roentgenologic picture of rickets is always preceded by roentgenologically observable changes, which are capable of being influenced by antirachitic treatment and which are interpreted as rachitic. The early changes are: General decalcification, decreased density of the calcification zone, and metaphysial sclerosis. They occur most often in conjunction, and are complementary to each other. The ribs are not suitable for the early roentgen diagnosis of rickets. These roentgenologic changes can always be seen earlier than the usual clinical ones, with the common exception of craniotabes. During the first weeks of life metaphysial decalcification occurs which, at least for the present, is not considered a rachitic sign."

McCUNE, New York.

VITAMIN C STANDARDS AND HYPOVITAMINOSIS: IV. COMPARATIVE INVESTIGATIONS CONCERNING SINGLE DETERMINATIONS OF THE BLOOD ASCORBIC ACID AND ASCORBIC ACID SATURATION TESTS. E. ERICSSON, Acta pædiat. **26**:140, 1939.

A comparison of peroral and intravenous saturation tests with the results of casual measurement of the ascorbic acid in the blood indicated that (1) the latter supplies highly useful information concerning the repleteness or deficiency of the body with reference to vitamin C and that (2) in the case of persons who have comparable blood levels knowledge more accurate than that obtained by casual examination of the blood can be secured by intravenous saturation, 100 mg. of ascorbic acid being used and the concentration in both blood and urine being measured. The method is particularly informative in the presence of severe deficiency; it is recommended because of its ease of execution.

McCUNE, New York.

THE VITAMIN C CONTENT OF BREAST MILK IN GOTHENBURG. E. GEDDA and K. KJELLBERG, Acta pædiat. **26**:177, 1939.

An investigation of the vitamin C content of the breast milk of 421 Swedish women was carried out during autumn and spring. The titration of vitamin C was made by Bessey's modification of Tillmann's method. The average value was 3.9 ± 0.07 mg. per hundred cubic centimeters. The vitamin C content was 0.6 ± 0.13 mg. higher in the autumn than in the spring.

McCUNE, New York.

RICKETS AMONG THE CHILDREN OF THE NOMADIC LAPPS. G. GEZELIUS, Acta pædiat. **26**:184, 1939.

A physical and roentgen survey of the children in a tribe of nomadic Swedish Lapps revealed that rickets was present in 50 per cent of a group of 24 infants between 6 months and 1 year of age and in 42 per cent of 69 children aged 1 to 3 years. The explanation is offered that the Lapp babies suffer from lack of ultraviolet light during the first year of life and do not receive vitamin D.

McCUNE, New York.

VITAMIN C STANDARD AND HYPOVITAMINOSIS: I. THE VARIOUS METHODS FOR DETERMINING THE OPTIMUM REQUIREMENT OF VITAMIN C AND FOR DEMONSTRATING HYPOVITAMINOSIS. M. ODIN, Acta pædiat. **26**:339, 1939.

The determination of the optimum intake of vitamin C depends on the successful solution of the problem of recognizing mild grades of deficiency. To this end the following methods can be employed: surveys of the dietetic history of individual patients or groups; determination of the concentration of ascorbic acid in the blood; saturation procedures of various sorts that involve chemical measurement of vitamin C; studies of capillary fragility; dental roentgenograms, and, finally, histologic examinations of extracted teeth. Each method has its advantages and limitations. The author discusses these in detail, bringing to the subject the authority of one who has worked in the field for a long time.

McCUNE, New York.

VITAMIN C STANDARD AND HYPOVITAMINOSIS: II. THE DETERMINATION OF ASCORBIC ACID WITH THE PHOTOELECTRIC CELL. M. ODIN, Acta pædiat. **26**:351, 1939.

The method depends on the reductive decolorization of methylene blue. The colorimeter employs a barrier layer photoelement. A red filter is used, the absorption curve of which is not reproduced. Parallel determinations exhibit high agreement.

McCUNE, New York.

VITAMIN C STANDARDS AND HYPOVITAMINOSIS: III. DIET, BLOOD ASCORBIC ACID AND CAPILLARY BLEEDING TESTS. T. THYSELL, Acta pædiat. **26**:481, 1939.

In 634 cases a history of dietary habits was elicited, the blood ascorbic acid measured and a test of capillary bleeding carried out. A comparison of the results of the three types of examination demonstrated that knowledge of a person's habitual diet provides the means for making a dependable estimate of that person's repletion with or lack of vitamin C, as judged by the level of ascorbic acid in the blood. The value of tests of capillary fragility has been considerably overestimated.

McCUNE, New York.

Prematurity and Congenital Deformities

MUSCULAR AND SKELETAL CHANGES IN ARACHNODACTYLY. JOHN J. FAHEY, Arch. Surg. **39**:741 (Nov.) 1939.

The syndrome designated as arachnodactyly was first described in 1896. In this condition there is either actual or apparent lengthening of the hands and feet, particularly the fingers and toes. The face may have an appearance of maturity because of a decrease of subcutaneous tissue. Skeletal development is in advance of chronologic age in many cases. The soft tissue about the extremities is poorly developed. There are ligamentous relaxation and occasionally contractures of the fingers. Spinal curvature in early childhood is common. The intelligence in most instances is normal. The condition may be spasmodic or familial. Dislocation of the lenses associated with other ocular anomalies has been found in over half of the reported cases. The abnormalities associated with arachnodactyly are not ordinarily detected until the second or third year of life.

The author describes this condition accurately, adding 6 cases to the reported ones. The treatment consists in correcting the myopia and astigmatism with suitable lenses or in the removal of the lens if it is completely dislocated. The finger contractures may be treated, with improvement in function.

KAISER, Rochester, N. Y.

A CASE OF INTRAPARTUM FOETAL DEATH DUE TO INTRA-UTERINE RUPTURE OF THE UMBILICAL VEIN. D. FRIEDLANDER, J. Obst. & Gynaec. Brit. Emp. **47**:334 (June) 1940.

A case is described of intrauterine death of the fetus due to spontaneous rupture of the umbilical vein in a normally formed umbilical cord. Hemorrhage into the amniotic sac occurred. The mother was perfectly well throughout the antepartum period. It is suggested that the rupture was due to an intrauterine infection occurring during a prolonged labor. ADAIR and POTTER, Chicago.

CONGENITAL FACIAL HEMIHYPERTROPHY WITH OCULAR ANOMALIES: REPORT OF TWO CASES. R. GOZBERK, Ann. d'ocul. **176**:624 (Aug.) 1939.

Congenital facial hemohypertrophy is a rare condition. The writer gives a report of the work of Sabrazes and Cabannes, who in 1898 found 18 cases in the literature, some of which, however, were rather indefinite. The last case noted was presented before the Société française d'ophtalmologie in 1931.

Gozberk gives the details of 2 cases, illustrated with photographs. One patient was a girl of 10 years and the second a child of 2 years.

The chief details of the subject are summarized—etiology, pathologic anatomy, pathogenesis, symptoms and diagnosis. S. H. McKEE. [ARCH. OPHTH.]

CONGENITAL CATARACTS AND OXYCEPHALY. G. P. SOURDILLE, E. DUVAL and GENDRON, Bull. Soc. d'opht. de Paris **51**:186 (March) 1939.

In a recent thesis Lartigue has shown the rarity of congenital cataracts associated with oxycephaly. Two observations are cited. A girl 7 years of age was born at six and one-half months. A cranial deformity was noted. Vision had always been poor. Both lenses had lamellar cataracts. The hands and feet had the classic aspect of arachnodactylia. The roentgenograms of the skull showed signs of hypertension with digital impressions on the convexity of the skull. Examination of the fundi after operation for the cataracts failed to reveal any change from the normal.

The second patient was 5 years of age. The family history showed no hereditary stigmas. The patient was thought to have normal vision as a baby. In later years it was found to be deficient. Lamellar cataracts were discovered. A roentgenogram of the skull was characteristic of oxycephaly. After operation for the cataracts the papillae were found to be edematous with congested borders. Pictures and roentgenograms are included.

L. L. MAYER. [ARCH. OPHTH.]

A CASE OF CONGENITAL ANOMALY IN A CHILD OF NINE YEARS. N. VACAREANU, Bull. Soc. de pédiat. de Iasi **10**:12, 1939.

The author presents the case of a boy who showed aplasia of the pectoral muscles, the serratus magnus muscle and the sternal portion of the first three intercostal muscles on the right side. There was also pronounced atrophy of the right arm.

LESLIE, Evanston, Ill.

SYNDACTYLY WITH CAMPTODACTYLY: TREATED ON THE RIGHT BY FREE TOTAL SKIN GRAFT, ON THE LEFT BY THE USUAL METHODS. MARCEL FÈVRE, Bull. Soc. pédiat. de Paris **37**:186 (April) 1939.

Free total skin grafting is considered the method of choice, and it allows early surgical correction.

BENJAMIN, Montreal, Canada.

TWO CASES OF DOLICHOSTENOMELIA. ASSOCIATION IN ONE CASE WITH LOBSTEIN'S DISEASE. G. BOUDET, J. BALMÈS and J. BARNAY, Bull. Soc. pédiat. de Paris **37**:188 (April) 1939.

A 15 year old boy had long, thin extremities. He had suffered eight fractures since infancy. The value for blood calcium was 6.5 mg. per hundred cubic centimeters. A boy of 13 years had a level of blood calcium of 15 mg. per hundred cubic centimeters.

BENJAMIN, Montreal, Canada.

A CASE OF FAMILIAL CRANIOFACIAL DYSTROPHY. A. AUSTREGESILO, Rev. neurol. **72**:165 (Aug.) 1939.

A typical case of oxycephaly is presented. Two sisters showed similar changes in the osseous development of the skull.

DAFFINEE, Boston.

THE GASTRIC AND DUODENAL SECRETIONS OF IMMATURE INFANTS. A. GALEOTTI FLORI, Riv. di clin. pediat. **38**:193 (April) 1940.

Observations on the duodenal secretions of 3 immature infants 2 weeks old and weighing from 3¼ to 4¼ pounds (1,420 to 1,927 Gm.) revealed a tryptic activity normal for infants; lipase was a little diminished, and amylase was absent.

Observations of the gastric juice were made with 25 immature infants; free hydrochloric acid was not found, except for traces in 3 infants; only 9 infants showed any total gastric acidity; 11 showed the presence of some rennin, and only 2 showed a normal amount.

HIGGINS, Boston.

CAMPTODACTYLIA (CONTRACTURE) IN CHILDREN. JULES R. DREYFUS, Jahrb. f. Kinderh. **148**:336 (March) 1937.

Illustrations are given showing patients with this type of abnormality, which consists typically of congenital contracture of the little finger of one or both hands. Numerous instances are cited in which several members of different generations were afflicted.

Orthopedic treatment, usually surgical, is indicated.

LANDAU, Hannibal, Mo.

FETAL PELVIS. H. YAMAMURA, Jap. J. Obst. & Gynec. **22**:288 (Oct.) 1939.

The paper consists of many measurements of fetal pelves, all of which have been subjected to considerable statistical analysis. A description of the histologic development of pelvic bone is included.

ADAIR and POTTER, Chicago.

THE OUTCOME OF HOSPITAL CARE OF 114 IMMATURE INFANTS AND THE COURSE OF THEIR DEVELOPMENT DURING THE FIRST YEAR OF LIFE. G. MÜHL, Acta pædiat. **26**:301, 1939.

This study describes the course in the hospital and the subsequent history of 114 infants whose birth weight was under 2,500 Gm. The immediate mortality was 12.3 per cent. The infants whose birth weight was under 2,000 Gm. developed more slowly than did those whose weight was above 2,000 Gm. The members of the latter group appeared to develop in a normal manner. Follow-up inquiry revealed that the incidence of physical and mental defect from various causes was not higher than one might expect to find in normal children.

McCUNE, New York.

Newborn

SERIAL BLOOD SUGAR DETERMINATIONS IN NORMAL NEWBORN INFANTS. JOHN B. McKITTRICK, J. Pediat. **16**:151 (Feb.) 1940.

Determinations of the values for blood sugar were made for 73 normal newborn infants and 1 infant of a diabetic mother. During the first week of life low values were found. The lowest point was reached by the average baby on the third day. Values for blood sugar above 40 mg. per hundred cubic centimeters were regarded as normal in the first week of life. During the second week the range was found to be from 60 to 120 mg., with the average between 80 and 90. During the first two weeks of life a gradual elevation of the level of blood sugar occurred, with a decrease in the spread of the maximum and minimum extremes. The blood sugar–regulating mechanism of the newborn infant is unstable and undergoes an alteration toward greater stability during the first two weeks of life.

RAUH, Cincinnati.

ICTERUS GRAVIS NEONATORUM. J. B. BILDERBACK and MORRIS J. BRIDGEMAN, Northwest Med. **39**:85 (March) 1940.

A review of 10 cases of erythroblastosis foetalis is given. A description of the clinical picture of congenital hydrops and icterus gravis, with a review of the literature, is included. The value of large intravenous transfusions is emphasized. The conditions described included mild, moderate and severe types. Six patients died.

ROBERTSON, Omaha.

SERUM VOLUME INDEX STUDIES ON NEWBORN CHILDREN. HENRY LEIDENHEIMER JR. and F. F. BOYCE, Proc. Soc. Exper. Biol. & Med. **43**:446 (March) 1940.

Blood from 6 white and 5 Negro mothers and their newborn infants was placed in a graduated cylinder, and the volume of serum expressed from the clot

was read at four hours. With normal persons the serum expressed is 50 per cent of the blood volume. The index equals the serum volume over one-half the volume of blood withdrawn. One (1) is a normal value. The highest index at which a jaundiced patient has bled is 0.71. The infants' indexes in this study were considerably lower than the maternal indexes. In 4 instances the infants' indexes fell to within the range in which bleeding would occur in adults. The authors feel that these studies confirm the work of others, who have found, using other tests, that a bleeding tendency exists in infants for a short time after birth.

HANSEN, Minneapolis.

A METHOD FOR INITIATING RESPIRATION IN THE NEWBORN. N. BOGRAD, South. M. J. **33**:531 (May) 1940.

The author states that stimulation by stroking the hard palate with gauze will reflexly contract the abdominal muscles and initiate respiration.

The method is superior to the older forms of stimulation, since it does not lead to excessive loss of heat, shock and other complications.

SCHLUTZ, Chicago.

STAPHYLOCOCCUS AUREUS INFECTION OF THE LONG BONES IN THE NEWLY BORN. JEAN M. CASS, Arch. Dis. Childhood **15**:55 (March) 1940.

Three cases of Staphylococcus aureus infection of the long bones in the newborn are reported and discussed. The condition is found to be compatible with a good general condition and a good ultimate prognosis, apart from the risk of deformity, if the infection is unmixed and if the lungs, skin, peritoneum and meninges are not involved. Repeated aspiration without open drainage gave good results, and the lesions healed rapidly without sequestrum formation.

KELLY, Milwaukee.

TETANY OF THE NEWBORN. JEAN LEVESQUE and SUZANNE DREYFUS, Bull. Soc. pédiat. de Paris **37**:243 (May) 1939.

An infant born by cesarean section was thought to have tetany. The spinal fluid showed an increased protein content. When observed later the infant was found to be a spastic idiot. It is emphasized that before a diagnosis of tetany of the newborn is made the spinal fluid should be examined to exclude the presence of intracranial abnormality.

BENJAMIN, Montreal, Canada.

VESTIBULAR FUNCTION IN THE NEWBORN. L. BALDENWECK and GUY-ARNAUD, Presse méd. **48**:47 (Jan. 16) 1940.

A series of observations on newborn infants confirmed the observation of other authors that the newborn child possesses a vestibular apparatus the function of which can be tested by the usual clinical methods. These methods may also be used to determine the presence of vestibular pathologic change in cases of otitis media, birth injury, congenital lesions of the vestibular apparatus or lesions of the central nervous system. The body musculature responds to the labyrinth reflexes; in fact, some birth injuries may involve the path of these reflexes. These body responses have been observed in fetuses as young as 2 months (Minkowski). The vestibular nerve is entirely formed by the second month of fetal life, and myelinization is complete at 4 months. As to the early appearance of the labyrinthine function, the authors hazard the opinion that the fetus is enabled by this function to maintain its proper position in utero.

DAFFINEE, Boston.

NUCLEAR ICTERUS OF THE NEWBORN. M. PÉHU and M. DOLLET, Rev. franç. de pédiat. **15**:349, 1939.

One is struck by the clarity of the writing of Péhu and his associates. Although there is considerable controversy concerning nuclear icterus, there is no confusion in the presentation of material. Various observed facts are laid before one. The picture is not yet complete, but one does not doubt that eventually it will be put together.

In résumé it is said that nuclear icterus represents an anatomicopathologic syndrome observed exclusively in the newborn. It is seen principally in cases of icterus gravis familiaris (Pfannenstiel). Clinically it is characterized by respiratory difficulties (dyspnea), difficulty in swallowing, lack of appetite, general apathy, somnolence and coma, all manifestations coming on in the course of icterus gravis familiaris and capable of leading to death in a few days.

Anatomically the condition is above all characterized by an intense yellow coloration of the centers of origin of the cranial nerves, with destructive cellular lesions distributed unequally throughout the nuclear groups.

When the acute phase has passed complete recovery is possible, but it usually happens that after several months the infant shows psychomotor retardation which resembles that associated with the chronic encephalopathies.

LESLIE, Evanston, Ill.

A CASE OF ICHTHYOSIS FOETALIS GRAVIS. O. C. POLI, Med. ital. **21**:1 (Jan.) 1940.

The author describes a case of fatal ichthyosis in an infant 1 day old. There is a detailed description of the autopsy and histologic observations. The author summarizes the principal hypotheses concerning the etiology of the disease.

MARTOCCIO, Utica, N. Y.

THREE CASES OF HEMORRHAGIC MENINGITIS IN THE NEWBORN. DAVID BERDEAL AVILA and DELIO AGUILAR GIRALDES, An. Soc. puericult. Buenos Aires **3**:285, (Oct.-Dec.) 1937.

The authors report 3 interesting cases of hemorrhagic meningitis in newborn babies, all of whom died at about the age of 2 weeks. Autopsy showed hemorrhages over one or both cerebral hemispheres. No bacterial cause was found.

HERRON, Oak Ridge, La.

ICTERUS GRAVIS AND CONGENITAL ANEMIA IN INFANTS. OTTO SAXL, Jahrb. f. Kinderh. **148**:271 (Feb.) 1937.

Histories are given of 10 cases of congenital anemia in the newborn. Included in this group are the cases of infants with sepsis, von Jaksch's disease, or infantile pseudoleukemia, syphilis, atresia of the bile ducts and melena. As all of the infants showed the clinical picture of congenital anemia, some of them with hydrops, the author concludes that congenital anemia of the newborn is not a clearcut clinical entity but may be brought on by a variety of causes. LANDAU, Hannibal, Mo.

HEMORRHAGIC DIATHESIS OF THE NEWBORN AND VITAMIN K. K. F. KOLLER and N. FIECHTER, Schweiz. med. Wchnschr. **7**:136 (Feb. 17) 1940.

K. F. Koller and N. Fiechter (Zurich) report that normally during the first weeks of life there is a retardation of coagulation, which is due to a lack of prothrombin. The disturbance in coagulation reaches a maximum three to five days after birth. There is, therefore, a physiologic transitory hypothrombinemia of the newborn.

In the hemorrhagic diatheses of this period (such as melena and cephalhematoma), which as a rule break out two to five days after birth, a heightening of the physiologic disturbance in coagulation can be demonstrated. Through the administration of vitamin K both the physiologic and the pathologic manifestations of the unduly delayed coagulation will be promptly influenced, and manifest hemorrhages can be controlled.

ABT, Chicago.

THE ROLE OF OBSTETRICS IN PRODUCING HEMORRHAGE IN THE LIVER IN NEWBORN INFANTS. H. FUJIMORI, K. MIZUNO and K. MENJU, Jap. J. Obst. & Gynec. **22**:390 (Dec.) 1939.

The authors examined 30 fetuses and infants at necropsy and in 11 found what is described as parenchymal or subserosal hemorrhage of the liver. It was frequently associated with intracranial hemorrhage and in general was believed due to the same causes. Difficult delivery was the principal etiologic factor.

ADAIR and POTTER, Chicago.

Acute Contagious Diseases

SMALLPOX IN SPANISH AND MEXICAN CALIFORNIA, 1770-1845. S. F. COOK, Bull. Hist. Med. **7**:153 (Feb.) 1939.

For almost three quarters of a century—1770 to 1830—California escaped serious epidemics of smallpox while the disease was rampant in other regions. This was due to the extreme isolation, the active preventive efforts of the government and the relatively early introduction of vaccination. The earliest reference to a possible epidemic dates from 1781. The author presents in extenso documentary material dealing with preventive measures, e. g., the royal edict of 1786, which was sent to the colonies with dissertations on the protection of the population from smallpox, and the edict of the viceroy Branciforte, of 1797, which was issued in an effort to prevent spreading of a severe epidemic in southern Mexico and Guatemala.

Vaccination was brought to the Spanish colonies in 1803 by Francisco de Balmis, a court physician. Part of his expedition touched United States territory in Texas, but its influence was felt in California. The clergy helped to spread the idea of vaccination, as is illustrated by the order of the bishop of Sonora to the president of the missions (1804), but it did not come into use until about 1817.

In 1828 the long regional immunity came to an end. The epidemic of 1828-1829 coincided with the first major attempts at wholesale vaccination, carried out by James O. Pattie, an American frontiersman. The author's critique of Pattie's claim that he vaccinated 22,000 persons is a scholarly piece of work; it convinces the reader that 3,000 to 6,000 comes closer to the truth.

Two more epidemics occurred in California before the Americans came, the "Miramontes epidemic" of 1838-1839 and the epidemic of 1844. The latter brought about the establishment of a hospital in Monterey and a board of health.

ROSENTHAL, St. Paul.

CHICKENPOX FOLLOWING CONTACT WITH HERPES ZOSTER. MAURICE L. BLATT, MARY ZELDES and ALBERT F. STEIN, J. Lab. & Clin. Med. **25**:951 (June) 1940.

Two minor epidemics of chickenpox following herpes zoster are reported. The point of difference from usual epidemics of chickenpox lay in the fact that few secondary infections occurred among the many children exposed.

READING, Galveston, Texas.

IMMUNITY TO THE LANSING STRAIN OF POLIOMYELITIS AS REVEALED BY THE PROTECTION TEST IN WHITE MICE. V. H. HAAS, Pub. Health Rep. **55**:1061 (June 14) 1940.

The Lansing strain of the poliomyelitis virus was used on white mice. An appreciable percentage (68.7 per cent) of the human serums protected mice against the virus. This protection increased with the age of the donors.

SANFORD, Chicago.

THE EPIDEMIOLOGY OF POLIOMYELITIS, WITH SPECIAL REFERENCE TO THE VICTORIAN EPIDEMIC OF 1937-1938. F. M. BURNET, M. J. Australia **1**:325 (March 9) 1940.

Burnet presents a fine general discussion of the results of his recent experimental investigations on poliomyelitis, the detailed accounts of which have been published elsewhere. The most important result of this work was to indicate (*a*) that infection in the epidemic did not produce poliomyelitis antibody, (*b*) that certain children with initial antibody nevertheless suffered from paralytic infection and (*c*) that cynomolgus monkeys could be infected with the local virus by ingestion or by pharyngeal swabbing. A discussion of the age incidence of poliomyelitis, of which there has been a rise in epidemics since 1930 so that in most communities there are now at least as many cases in the age group of 5 to 10 years as from nil to 5 years, leads to the conclusion that an important change in the character of the disease has taken place in the last thirty or forty years. The interpretation suggested is that in the earlier period poliomyelitis was essentially an adult infection with incidental involvement of infants, while epidemic poliomyelitis now is a disease of childhood, spread by child contact. The implications of this hypothesis in regard to the measures called for in the control of an epidemic are discussed and include restriction of the aggregation of children as much as social considerations will allow, isolation of known child "contacts" for three weeks and enforcement of a similar period of isolation for all children going from an infected to a noninfected community.

GONCE, Madison, Wis.

DIPHTHERIA PROPHYLAXIS IN INSTITUTIONS FOR CHILD CARE. P. LEREBOULLET, Paris méd. **2**:290 (Dec. 2-9) 1939.

The author concludes that the detection and treatment of diphtheria carriers in any institution caring for infants is of primary importance. Immunization is, of course, of great value, but if a carrier is present the disease may be acquired before immunization is possible. The author also emphasizes the importance of good hygiene and adequate diet.

LESLIE, Evanston, Ill.

MEASLES IN AN INFANT TWENTY-NINE DAYS OLD. M. PREBIL, Med. ital. **20**: 581 (Dec.) 1939.

An infant aged 29 days had measles and made a satisfactory recovery. The opinion is current that measles does not manifest itself before the fourth or fifth month. The author cites several reported cases in which measles occurred in younger infants. Measles probably develops in those infants whose mothers do not have specific antibodies in their blood.

MARTOCCIO, Utica, N. Y.

SCARLATINAL RHEUMATISM. F. BAZAN and R. MAGGI, Arch. argent. de pediat. **12**:376 (Oct.) 1939.

Scarlatinal rheumatism is influenced most favorably by two remedies, sodium salicylate and acetylsalicylic acid. The authors recommend from 2 to 6 Gm. of the former daily for the child. The remedy is well tolerated and usually causes a disappearance of the painful arthritis.

There is no ill effect on the kidney from the use of sodium salicylate, and it can be used even if some renal complication is present. Both remedies seem to act as preventives against possible complication of the heart.

If acetylsalicylic acid is used, 0.25 to 1 Gm. daily is given the child under 8 years of age; for children from that age to 14 years the dose can vary between 1 and 3 Gm. daily.

SCHLUTZ, Chicago.

ANTIDIPHTHERIA IMMUNIZATION. R. AGUIRRE and J. SAGUIER, Arch. argent. de pediat. **12**:497 (Nov.) 1939.

The authors criticize the public apathy which exists toward general immunization against diphtheria. This is common in the Argentine republic as well as in other countries.

The authors advocate the passing of laws which will compel immunization. Its value in reducing mortality from diphtheria has been so overwhelmingly proved that they feel that any government which does not bring about compulsory immunization is failing grievously in its duty toward the general public.

SCHLUTZ, Chicago.

VARICELLA ENCEPHALITIS. J. L. DEAL and F. M. GASTELU, Arch. de pediat. d. Uruguay **10**:620 (Oct.) 1939.

The authors report the occurrence of this condition in a child 3½ years old. It was the fourth case reported in Argentina and Uruguay.

The predominating symptoms were static tremor of the lower extremities, loss of equilibrium and marked nystagmus.

Complete recovery occurred on the fifteenth day after the onset.

SCHLUTZ, Chicago.

OBSERVATIONS ON INFANTILE PARALYSIS. PABLO MENDIZABAL, Rev. mex. de pediat. **9**:384 (Aug.) 1939.

The author gives a good general review of the subject, using a great many references by American authors. He reports no specific cases, but the review is well done.

HERRON, Oak Ridge, La.

STOMATITIS AND INFECTIOUS DISEASES. HERMANN ZISCHINSKY, Jahrb. f. Kinderh. **149**:40 (April) 1937.

Numerous cases of infections of the mouth are reported, including gingivitis in cases of whooping cough, ulcerative stomatitis associated with the same condition and aphthous stomatitis in cases of scarlet fever and pertussis. Aphthous stomatitis was also found in cases of diphtheria and measles. Various other forms of oral infection were associated with the infectious diseases. Detailed descriptions of the different types are given. There seem to be but fine shades of difference between many of those listed. Many of the infectious diseases are accompanied by oral infections in numerous instances.

LANDAU, Hannibal, Mo.

ACUTE INSUFFICIENCY OF THE SUPRARENAL CORTEX FOLLOWING SCARLET FEVER. J. W. CAMERER, Jahrb. f. Kinderh. **149**:66 (April) 1937.

Symptoms of insufficiency of the adrenal gland developed in a child of 3 years and 2 months, fourteen days after a comparatively mild attack of scartet fever.

His appetite was poor; there was frequent vomiting, and he was in a state of exhaustion. There was considerable loss of weight, besides ulcers in the mouth and swelling of the gums. The skin was pale. The reaction to tuberculin was consistently negative.

The diagnosis of adrenal insufficiency was made, and treatment was started with intravenous dextrose, cortical extracts and a blood transfusion.

The patient had three acute crises, during which the classic symptoms were accentuated. Cardiac stimulants and the usual heroic measures failed to bring him out of the third crisis.

Postmortem examination showed widespread fatty necrosis of the cortex in both adrenal glands, with a similar, but not so marked, change in the medullary portions.

LANDAU, Hannibal, Mo.

IS SERUM EFFECTIVE IN CASES OF DIPHTHERIA GRAVIS? H. MÜLLER and H. SEIDLMAYER, München. med. Wchnschr. **86**:1297 (Aug. 25) 1939.

The authors state that it may seem laughable to some that in these days one still discusses and investigates the value of serum in treatment of diphtheria. They point out that some leading clinicians, e. g., Zischinsky, of Vienna, and Hottinger, of Düsseldorf, as well as many of lesser reputation, have seriously questioned the efficacy of diphtheria serum. They also call attention to the fallacy of presenting preserum results when only the fatality percentages are given. For example, Kohts reported the following mortality rates according to the day on which treatment (without serum) was begun: first day, 100 per cent; second day, 80 per cent; third day, 53 per cent; fourth day, 46 per cent, and fifth day, 31 per cent—a surprising result. But one finds that in the original article Kohts was reporting 100 cases of tracheotomy, in only 16 of which treatment was given on the first two days. Glaeser also reported results in the preserum days, with the following mortality rates according to the day of treatment: 40, 20, 25, 38, 30 and 21. This report includes all cases of diphtheria and gives no inducement to dispense with serotherapy at present.

The authors report the results for 377 patients with diphtheria gravissima, or hypertoxic diphtheria, treated at the University Hospital in Munich during the last fifteen years. The results are similar to those of most reports, the mortality rate steadily rising as serum treatment was delayed. The mortality rate for the patients treated within three days was 41 per cent and for those treated after the third day was 71 per cent. The authors also collected 580 cases of hypertoxic diphtheria reported in the literature and found that the trend of the mortality rate in the group as a whole was similar to that in their own series.

BRAHDY, Mount Vernon, N. Y.

SIGNIFICANCE OF THE ELECTROCARDIOGRAM DURING THE FIRST DAYS OF DIPHTHERIA. LADISLAV SYMON and MARIE FIRYT, Časop. lék. česk. **76**:790 (June 22) 1937.

According to the literature the pathologic electrocardiographic findings may antedate the positive clinical findings by as much as ten days in showing the development of myocarditis. The most common observation is a diphasic, a normal or a missing T wave in the third lead. The next most common is a change in the QRS complex in the third lead. Of 18 cases studied in which the condition was mild, in 11 there were electrocardiographic changes, in 2 the findings were indefinite and in 5 no changes were revealed; of 7 cases in which the disease was moderately severe, in 6 there were electrocardiographic changes and in 1 the reading was normal; of the 9 cases of severe myocarditis, in 7 there were definite changes and in 2 normal findings, while in the fatal case there were definite changes. A normal T wave in the third lead with a right preponderance is considered indicative of grave prognosis. In 1 case of frank myocarditis the electrocardiographic findings were normal. The author feels that the electrocardiogram is most valuable in revealing the myocardial changes found early in the cases of apparently mild disease.

STULIK, Chicago.

POTASSIUM CHLORATE IN TREATMENT OF ACUTE ANTERIOR POLIOMYELITIS. H. J. KOLK, Nederl. tijdschr. v. geneesk. **84**:388 (Feb. 3) 1940.

Kolk directs attention to Contat's method of chemotherapy for poliomyelitis. Although this method of oral administration of potassium chlorate is still under investigation the author thinks that the results he obtained with it justify calling attention to this procedure. The daily dose for each patient is determined on the basis of 100 mg. per kilogram of body weight. Thus, for an infant of 4 Kg. the daily dose is 0.4 Gm., whereas for a child of 20 Kg. it is 2 Gm.; the daily dose should not exceed 8 Gm. The drug is administered by mouth every two hours day and night, each individual dose constituting one twelfth of the total daily dose. If the same daily dose is given in larger fractions at less frequent intervals, there is danger of toxic effects. In addition to the oral medication the patients are given nasal instillations of 5 drops of a solution of potassium chlorate in each nostril four times a day. After two days the oral dose is reduced by omitting one daily and one nocturnal administration, and after six days the chemotherapy is stopped. The author treated some of the patients with potassium chlorate and serum and others with potassium chlorate alone. In all, the potassium chlorate therapy was used in 52 cases, and the impression was gained that the progress of the paralytic symptoms was arrested and that in the preparalytic stage paralysis was prevented.

J. A. M. A.

Acute Infectious Diseases

EFFICACY OF GENTIAN VIOLET IN THE TREATMENT OF PINWORM INFESTATION. WILLARD H. WRIGHT and FREDERICK J. BRADY, J. A. M. A. **114**:861 (March 9) 1940.

With use of a special swab, repeated scrapings about the anal areas revealed oxyuriasis. The method of treatment with gentian violet, orally administered, is described, and the results are given as checked by the cellophane swabs. The authors found the method effective, cheap and applicable to the whole family. Toxicity was rare.

It is advisable to check for other parasites in the stools.

HEERSMA, Kalamazoo, Mich.

THE THERAPY OF FUSOSPIROCHETOSIS (VINCENT'S DISEASE). HENRY FIELD JR., J. A. M. A. **114**:1073 (March 23) 1940.

Field reviews the symptoms of this symbiotic infection with spirochetes and fusiform bacilli. Vitamin deficiency and other diseases may be associated, particularly avitaminosis C.

Involvement is usually in the gums or about the teeth but may also be tonsillar or pulmonary.

Treatment is varied but consists principally of the use of arsenicals internally or locally and oxidizing agents locally.

HEERSMA, Kalamazoo, Mich.

THE STREPTOCOCCAL ANTIFIBRINOLYSIN TEST IN CLINICAL USE. PAUL L. BOISVERT, J. Clin. Investigation **19**:65 (Jan.) 1940.

This report summarizes the results of repeated streptococcic antifibrinolysin tests in 15 normal infants and children, 6 newborn infants and 203 patients of the pediatric age group. The observations suggest that while a single test may be of no certain diagnostic value, the trend of several tests may be significant. Positive results were obtained for 67 of the 75 patients with hemolytic streptococcic infections at some time during the course of their illness and convalescence. In 53 of 70 patients with primary hemolytic streptococcic infections the result was negative during the acute phase of the disease but became positive about the time of recovery.

GUEST, Cincinnati.

ON THRUSH, WITH SPECIAL REFERENCE TO VAGINAL THRUSH. W. GLEN LISTON and LEWIS G. CRUICKSHANK, Edinburgh M. J. **47**:369 (June) 1940.

The authors begin with the statement that "any housewife knows that thrush is a condition which affects the mouths of suckling infants and old persons suffering from debilitating diseases."

There is first a discussion of the parasite of thrush as to nomenclature and differentiation from other organisms. Oidium albicans is the cause of thrush, whether it occurs in the vagina, the mouth or the skin.

The authors report 49 vaginal infections in a series of 200 consecutive pregnant women suffering from leukorrhea. The diagnosis is suggested by the history; thrush is seldom diagnosed by any vulvar manifestations but is discovered by examination of the vagina by speculum. Films were made and stained by the Gram method. The technic of examining films is thoroughly discussed.

The disease should be sought in the pregnant mother in order to safeguard the baby from infection at birth. NEFF, Kansas City, Mo.

ANEMIA OF LEISHMANIASIS. GIULIO MURANO and FEDERICO VECCHIO, Pediatria **47**:545 (July) 1939.

Twelve cases of leishmaniasis in children are presented. Examination of the blood showed a very low hemoglobin concentration, leukopenia, a low platelet count and a low red blood cell count. The authors speculate as to the cause of the anemia. MARTOCCIO, Utica, N. Y.

RHEUMATIC MEDIASTINITIS. J. C. BERTRAND and E. KIRCHMAYR, Arch. argent. de pediat. **11**:281 (March) 1939.

The authors report the occurrence of this rare condition in a girl aged 8 years. A mediastinal enlargement was demonstrated by roentgen ray technic.

The intensive use of the salicylates for about three weeks effected a complete cure of the condition. SCHLUTZ, Chicago.

ACUTE PSEUDO APPENDICULAR ABDOMINAL SYNDROME OF RHEUMATIC ORIGIN. E. A. BERETERVIDE, J. J. REBOIRAS and R. BEAUTEMPS, Arch. argent. de pediat. **12**:518 (Nov.) 1939.

The authors report 2 cases in which this peculiar train of symptoms was present, in connection with other manifestations of rheumatism. The disorder was relieved by intensive use of the salicylates.

The abdominal symptoms were so severe that an acute attack of appendicitis was simulated.

The authors caution, however, that intervention such as that described should always be practiced in any case in which there is the least doubt.

SCHLUTZ, Chicago.

BACILLARY DYSENTERY IN RELATION TO THE SUMMER DIARRHEA OF INFANCY. H. HORMAECHE, N. SURRACO and P. L. ALEPPO, Arch. de pediat. d. Uruguay **10**:573 (Oct.) 1939.

Bacillary dysentery is endemic in Uruguay and is more common in the summer than in the winter.

The authors reported 224 cases of dysentery in which 196 of the patients were between the ages of 3 and 12 years and 52 were under the age of 3 years. There was no mortality among the patients above 3 years of age. Among the 157 patients under 3 years of age there were 54 deaths. Sixty of the children showed diarrhea due to Salmonella. SCHLUTZ, Chicago.

PROTEUS SEPTICEMIA IN A CHILD OF THREE MONTHS. G. C. PENICHET, B. D. CASTILLO and J. A. M. CRUZ, Bol. Soc. cubana de pediat. **11**:718 (Dec.) 1939.

In instances of certain forms of choleriform diarrhea, it is possible to isolate such well known organisms as Salmonella and Proteus. In these cases septicemia is often present.

The authors suggest that such a condition, which seems to be solely enteric diarrhea, is in reality septicemia.

Sulfanilamide seemed to be effective in the case reported by the author. It was given in connection with blood transfusions. SCHLUTZ, Chicago.

RENAL IRRITATION IN RHEUMATIC FEVER IN CHILDHOOD. HERBERT NATHHORST, Ann. pædiat. **155**:285 (July-Aug.) 1940.

Among 430 cases of acute rheumatic fever in children the author discovered 8 cases of acute hemorrhagic nephritis, which are reported in this paper.

The deposit of the urine of 35 children was examined quantitatively according to the method of Addis. In 50 per cent of cases an ordinary subclinical irritation of the kidneys could be found. This renal irritation was benign in all the cases and passed off quickly. The author states the opinion that it is probably allergic and can be compared most nearly to the polyarticular symptoms.

EDITOR'S SUMMARY.

EXPERIENCES WITH SULFONAMIDE COMPOUNDS IN GONORRHEA. A. NORDENSKJÖLD, Acta pædiat. **26**:325, 1939.

This report is not concerned with children but describes the treatment of gonorrheal infections in men and women and supplies statistics relating to the effect of treatment. McCUNE, New York.

A CASE OF EPIDEMIC ICTERUS (EPIDEMIC HEPATITIS) WITH AUTOPSY. P. SELANDER, Acta pædiat. **26**:451, 1939.

An addition is made to the small number of anatomic data relating to "catarrhal jaundice." A 5 year old girl, a resident of an apartment house in which an epidemic involving nearly 30 persons was in progress, sickened and died of epidemic jaundice. The terminal symptoms were those of hemorrhagic encephalopathy. Autopsy revealed diffuse hepatitis with swelling and fatty degeneration of the liver cells; in addition, cellular infiltration and evidence of early regeneration of the parenchyma were present. The portal lymph nodes were much altered. The brain could not be examined. The twin brother of the patient survived the infection.

McCUNE, New York.

Chronic Infectious Diseases

TUBERCULIN AND X-RAY SURVEY. W. PALMER DEARING, Am. Rev. Tuberc. **40**:640 (Dec.) 1939.

This survey was made in one county in Tennessee. About 3,000 children and 1,500 adults were examined. Tuberculin tests were done by the Mantoux method, with a single dose of 0.0005 mg. of purified protein derivative (one tenth of the official second strength dose). Flat anteroposterior roentgenograms of the chest were made and read by one physician, who had no knowledge of the other observations. The incidence of reaction to the tuberculin test was low during the first decade, and was well under 20 per cent at high school age. It arose more rapidly during the third decade and reached 70 per cent or more in old age.

Definite calcification, regarded as healed primary tuberculosis, was found to develop at an early age; the incidence in the age group from 5 to 9 years was 27 per cent for boys and 31 per cent for girls.

In the older age groups calcification was less frequently observed. This would indicate that the process was not progressive but the response to tuberculosis of the first infection type, and that some of the lesions may be resorbed with age. The percentage of persons of all ages showing calcified areas in the lungs was 31.8 and 36.8 for males and females respectively. The number of films showing calcification without manifest tuberculosis was 1,478, of which 35.4 per cent were those of persons who reacted positively to tuberculin and 34.2 per cent were those of persons who reacted negatively to tuberculin. This high incidence of calcification among persons showing negative tuberculin reactions raises the question of the specific cause of the condition. Analysis of the character and location of the lesions and comparison of these findings with those of known causation seem to the author definitely to indicate that the calcification in these persons was due to tuberculosis.

In the roentgenograms of 57 tuberculin-tested subjects there were found shadows regarded as indicating tuberculosis of the reinfection type. Of this number, 10 were nonreactors and 47 reacted positively to the Mantoux test. Subsequently, of the 10 nonreactors 1 was determined to be nontuberculous and another to have epituberculosis, since the lesion disappeared entirely. The final diagnosis in the remaining 8 cases was tuberculosis of the reinfection type.

In conclusion Dearing states that single dose Mantoux testing as described is a reasonably efficient diagnostic method, but roentgen study is still the basic tool for this purpose.

EUGENE H. SMITH, Ogden, Utah.

MASS TUBERCULIN TESTING AND X-RAYING. CHARLES L. IANNE, Am. Rev. Tuberc. **40**:654 (Dec.) 1939.

In planning procedures for the prevention of tuberculous infection, Ianne suggests that a logical place to start would be with the prospective mother. Preventive measures could easily be carried out in both clinics and private practice, with slight expense. The cost of fluoroscopic or roentgen examination for persons who react positively to tuberculin would be little more than that of routine Wassermann tests. Forty-one per cent of patients who returned for reading (to the Santa Clara County [California] Hospital) had positive reactions to tuberculin tests, and active tuberculosis was found in 1.7 per cent. Early diagnosis permits treatment of the mother when indicated, makes possible the safeguarding of the offspring and may lead to the detection of other cases in the family. "Prevention of tuberculosis should begin before birth."

EUGENE H. SMITH, Ogden, Utah.

FATEFUL PERIODS IN THE LIFE OF THE TUBERCULOSIS-INFECTED INDIVIDUAL. JULINS HOLLO, Am. Rev. Tuberc. **40**:659 (Dec.) 1939.

The fate of the tuberculous person in a civilized environment depends largely on his behavior during certain (mostly short) periods in his life. The decline in death rates from tuberculosis is not due primarily to new developments in therapy. Neither does the decrease in the number of infected persons account for the lower mortality. The course of tuberculosis as a chronic infection has become milder with the passage of time. In human beings living under normal physiologic conditions the disease does not as a rule involve serious danger to health. In Hollo's opinion the change is largely due to the greatly improved environmental conditions under which the bulk of the population now lives. If from any cause this favorable environment ceases to exist, resistance is likely to be broken down and the disease to progress. The chief catalysts in this process are malnutrition, overexertion and lack of fresh air.

The fateful periods in the life of the patient with tuberculosis are three, infancy, adolescence and old age. In infancy the yearly fatality rate is high. This is due to many factors besides low resistance to disease. Infections at this time are likely to be intradomiciliary and massive. Added to this in many instances are malnutrition and poor hygienic surroundings.

With adolescence many new factors confront the infected person. Parental supervision is relaxed; school and college responsibilities increase. Athletics and other forms of physical exertion are often indulged in to excess. To these external factors, rather than to increased susceptibility, a relatively large number of cases of tuberculosis owe an acute development during this period.

Contrary to the common belief, old age is remarkably defenseless against tuberculosis. In this fact are involved such factors as defective nutrition, indoor life, psychic depression and intercurrent disease. But the main cause is the decreased resistance of the old organism.

On the basis of these observations it appears that the normal periods of civilized life do not involve any material danger of activating a quiescent tuberculous focus. The dangers and harms are confined to comparatively short periods of life and thus frequently can be avoided by caution and care.

EUGENE H. SMITH, Ogden, Utah.

THE VOLLMER PATCH TEST AS A ROUTINE PROCEDURE. JOHN DORSEY CRAIG and LEWIS A. SCHEUER, Arch. Pediat. **57**:177 (March) 1940.

Two hundred and twelve children who had previously reacted positively to a 1:1,000 dilution of old tuberculin were tested with the Vollmer patch test and the first strength purified protein derivative. Two hundred and two, or 95.1 per cent, showed a conformity in positive reactions between the 1:1,000 dilution of old tuberculin and the Vollmer patch test. One hundred and eighty, or 84 per cent, showed a conformity in positive reactions between the 1:1,000 dilution of old tuberculin and the first strength purified protein derivative. The greatest number of negative reactions of the first strength purified protein derivative occurred in the children who had had a positive reaction to the old tuberculin an appreciable length of time before the testing.

The authors conclude that the Vollmer patch test is a satisfactory diagnostic mechanism.

ORR, Buffalo.

TUBERCULOSIS IN CHILDREN. CONSIDERING CONTACT IN THE DOMESTIC SERVANT. E. T. McENERY, Illinois M. J. **76**:559 (Dec.) 1939.

The importance of contacts with school teachers and domestic servants as sources of tuberculous infection in children is emphasized. Ways and means of providing greater protection to children are discussed. The county medical society, roentgenologists, physicians and education are important factors in such a campaign.

BARBOUR, Peoria, Ill.

THE PROTECTION OF CHILDREN FROM TUBERCULOUS ADULTS. FAIRFAX HALL, J. A. M. A. **113**:1873 (Nov. 18) 1939.

In order to protect children from tuberculous infection and reinfection, investigation must be directed particularly to school teachers and members of the household. The author reviews what has been done in this direction and emphasizes the high incidence of evidence of tuberculosis (positive Mantoux reaction) in children coming in contact with persons having the disease in an active form. If initial and periodic health examinations were urged or required for the transmitting group a tremendous step forward would be achieved.

HEERSMA, Kalamazoo, Mich.

CONGENITAL SYPHILITIC SYRINGOMYELIA WITH ARTHROPATHY OF ELBOW. PETER G. DENKER and FOSTER KENNEDY, J. A. M. A. **114**:408 (Feb. 3) 1940.

The case of a 12 year old boy is reported.

HEERSMA, Kalamazoo, Mich.

A Study of 1,852 Chest Roentgenograms of Tuberculous Contacts Under the Age of Five Years. Harold A. Rosenberg and Milton I. Levine, J. Pediat. **15**:224 (Aug.) 1939.

Rosenberg and Levine give the following summary of their observations:

"A study of 1,852 chest roentgenograms on 584 infants from tuberculous homes varying in age from birth to five years is presented.

"Among 379 cases with negative Mantoux tests, the incidence of tracheobronchial shadows alone was 6.8 per cent. The incidence of parenchymal shadows was also 6.8 per cent.

"Among 205 cases with positive Mantoux tests, the incidence of tracheobronchial shadows alone was 9.2 per cent; the incidence of parenchymal shadows was 40 per cent.

"Increased tracheobronchial shadows persisted more than three months in 26.6 per cent of the negative Mantoux cases, as against 71.3 per cent of the tuberculin-positive cases.

"Parenchymal shadows persisted on subsequent examination for three months or more in 8 of 16 (50 per cent) of the negative Mantoux cases, and in 61 of 66 (92.4 per cent) of positive tuberculin cases.

"Infants dying of tuberculosis generally show demonstrable parenchymal shadows on a roentgenographic film. . . .

"Increased tracheobronchial shadows in infancy may not be accepted as pathognomonic of tuberculosis, even in the presence of a positive Mantoux test. It appears, however, that a great majority of the parenchymal lesions in tuberculin-positive infants are probably tuberculous in nature."

Rauh, Cincinnati.

The Vollmer Tuberculin Patch Test: Evaluation of Its Relative Sensitivity. James G. Hughes, J. Pediat. **16**:171 (Feb.) 1940.

One hundred children who reacted positively to the intradermal tuberculin test were tested with the Vollmer patch test. Seventy-eight of these reacted positively to the first strength solution of purified protein derivative, while 22 reacted positively only to the second strength solution. Of these 100 children, 89 reacted positively to the patch test and 11 reacted negatively. Hughes believes that these results give further basis to the belief that the patch test may be used in preference to the intradermal test with first strength solution of purified protein derivative but that the patch test is inferior to the intradermal test with the second strength solution. No significant reactions other than local phenomena were encountered when the patch test was used.

Rauh, Cincinnati.

A Congenitally Syphilitic Family. L. Babonneix, Bull. Soc. pédiat. de Paris **37**:241 (May) 1939.

In a previous communication 2 children of one family were reported as having saber shins. After carefully examining the roentgenograms the author states that in the younger child, who was 3 years old, the deformity of the tibias was due to rickets.

Benjamin, Montreal, Canada.

Familial Syphilis. Léon Babonneix and André Motte, Bull. Soc. pédiat. de Paris **37**:183 (April) 1939.

Of 8 children born to parents who were both syphilitic, some showed signs of congenital syphilis while others did not. Periods during which the parents received no specific treatment, as compared with others when they did, presumably accounted for the variation of manifestations in their offspring.

Benjamin, Montreal, Canada.

MEDIASTINAL AND SUBCUTANEOUS EMPHYSEMA DURING THE COURSE OF MILIARY TUBERCULOSIS. PRESENTATION OF ROENTGENOGRAMS. WEILL-HALLÉ, A. ABAZA and LOGEAIS, Bull. Soc. pédiat. de Paris **37**:275 (May) 1939.

A boy 2 years old, whose nutrition was very poor, reacted positively to a tuberculin test. No tubercle bacilli were demonstrated in washings from the stomach. A roentgenogram of the chest showed disseminated shadows in the lungs typical of miliary tuberculosis as well as an area of density in the right hilar region, which was interpreted as the primary lesion. He had mediastinal and subcutaneous emphysema, which was visible in another roentgenogram of the chest, taken twenty-four hours before death. Necropsy was not performed.

BENJAMIN, Montreal, Canada.

ANTITUBERCULOUS VACCINATION OF GUINEA PIGS WITH BCG BY THE MULTIPLE PUNCTURE METHOD OF ROSENTHAL AND BY SCARIFICATION OF THE SKIN. L. NÈGRE and J. BRETEY, Rev. de la tuberc. **5**:824 (July) 1939.

Two groups of guinea pigs were vaccinated by the multiple puncture method. In those of one group 30 punctures were made at one site, and in those of the other group two vaccinations of 30 punctures each were made. Eight days later about 50 per cent of the animals gave positive intradermal reactions. One month later 85.7 per cent of those who had received 60 punctures and 63.6 per cent of those who had received 30 punctures gave positive reactions.

After vaccination by scarification, 40 per cent gave positive reactions in eight days and 77.7 per cent after one month. EUGENE H. SMITH, Ogden, Utah.

TUBERCULOSIS. P. R. CERVINI and J. R. MENDILAHARZU, An. Soc. puericult. Buenos Aires **5**:98 (April-June) 1939.

The authors present four roentgenograms of tuberculosis in infants. They stress the importance of absolute separation from the source of the infection, but first this source must be accurately determined. HERRON, Oak Ridge, La.

IMPORTANCE OF GASTRIC LAVAGE IN THE DIAGNOSIS OF TUBERCULOSIS. R. C. AGUIRRE and J. A. TAHIER, Arch. argent. de pediat. **11**:257 (March) 1939.

The finding of tubercle bacilli in the gastric washing proves that the organisms have come from a pulmonary focus.

To produce contact infection by such an organism it is necessary that the Koch bacillus be demonstrated in the lungs. The authors are of the opinion that an infant showing bacilli in the material obtained by gastric lavage does not necessarily provide a danger of infection by contact.

The tuberculous infection is spread only if these patients cough or expectorate freely. SCHLUTZ, Chicago.

CONGENITAL SYPHILITIC PNEUMONIA IN THE NEWBORN. ANTONIO MOSCA and OLGA MONETTA, Rev. méd. latino-am. **25**:421 (Jan.) 1940.

Three forms of congenital pulmonary syphilis are recognized: (1) white pneumonia, or the pneumonia of Virchow, (2) interstitial pneumonia and (3) gumma. To this a fourth may be added, miliary syphilis, a variety of the gumma form. A case is reported in which necropsy was performed twenty minutes after birth. The infant showed edema of the legs and cyanosis of the extremities without external manifestations of syphilis. The mother's reaction to the Kahn test was 2 plus on the third day of the puerperium. At necropsy, aside from hypertrophy of the liver, the spleen and the wall of the right ventricle of the heart, the hepatization of the lung was noteworthy. Sections through the lung showed that the

usual fetal lobulations had disappeared because of extensive areas of diffuse granulation. Microscopically, areas of dense accumulations of cylindric cellular epithelium were observed, and the alveoli were obliterated by accumulations of histiocytes, lymphocytes, mononucleate giant cells and in some sections large amounts of lipoid, giving a more or less white color, depending on the fatty degeneration or infiltration. Adair in a series of 1,044 autopsies on fetuses or on newborn infants encountered congenital syphilis in 46 and pneumonia alba in 8 (17.3 per cent).

DWYER, Kansas City, Mo.

LATE HEREDITARY AURICULAR SYPHILIS. J. C. GROS, Vida nueva **41**:136 (March 15) 1938.

The author presents 5 cases of deafness due to congenital syphilis occurring in adults. He reviews the symptoms and the pathologic picture and says that the results of meager treatments are poor.

HERRON, Oak Ridge, La.

RELATION OF TUBERCULOSIS TO WHOOPING COUGH. VLADIMIR MIKULOWSKI, Jahrb. f. Kinderh. **148**:346 (March) 1937.

Characteristic changes occur in the lungs in many cases of pertussis. In a number of instances it is difficult to differentiate between tuberculosis, paravertebral infection of the lung, pleural infiltration and bronchitis.

During the course of pertussis, numerous small disseminated tuberculous foci are reported when roentgen studies are made.

In a certain per cent tuberculous foci are lighted up, giving rise to disseminated tuberculosis.

LANDAU, Hannibal, Mo.

USE OF PURIFIED PROTEIN DERIVATIVE IN THE TUBERCULIN PATCH TEST. GEORGE OUYANG, Chinese M. J. **57**:51 (Jan.) 1940.

This study comes from the department of health of Peiping Union Medical College. The testing of 290 school boys aged 6 to 16 years with purified protein derivative, both intradermally and by patch, gave 209 positive reactions by the intradermal method. Ninety-eight per cent of the same group had positive patch reactions. The amount given with the needle was usually 0.00002 mg. A satisfactory concentration for the preparation of the patch material was 2.5 per cent.

NEFF, Kansas City, Mo.

TRANSFUSION-SYPHILIS WITH WIDESPREAD OSTEOMYELITIS AND CUTANEOUS LESIONS OF AN ERYTHEMA MULTIFORME TYPE. H. C. PIAN and C. N. FRAZIER, Chinese M. J. **57**:301 (April) 1940.

The authors report on 2 Chinese patients, 1 a boy of 8 years, who were recipients of blood from a professional donor of three years' experience. This donor had no physical indications of disease and a negative Kline reaction of the blood immediately before these two transfusions.

Syphilitic lesions developed in the recipients. The donor was then reexamined, and it was learned that twenty days after the transfusions a penile sore had developed. The blood test gave a positive reaction.

Roentgen pictures of 1 of the recipients showed syphilitic destruction of bone in the skull and long bones before treatment, and a subsequent picture, five months after treatment, demonstrated the healing of the lesions, which was accompanied with residual thickening of the periosteum and the cortex.

The second recipient had multiple lesions of the periosteum and a rash resembling erythema multiforme.

The writers discuss the procedure for prevention of such a catastrophe and also the effect of the size of the inoculum and the route of the infection on its virulence.

NEFF, Kansas City, Mo.

THIRD GENERATION SYPHILIS. PAAVO MAIJALA, Acta med. Scandinav. **103**:1, 1940.

This is a report of a fairly authentic case. The grandmother admitted promiscuity in her early youth but was never aware of infection. She was always in "good health." She had one stillborn child, then five premature children, of whom only one survived, a daughter, who represents the second generation. She was very weak and from the age of 8 years suffered from dizziness and headache, worst at night. She always tired easily. The Wassermann reaction of the serum was doubtful and that of the spinal fluid negative (syphilitic vascular disease?). She had never had extramarital intercourse; her husband stated that he did not have syphilis; his Wassermann reaction was negative, and the physical examination presented no evidence of syphilis. Her 17 year old son represents the third generation. He had interstitial keratitis of one eye at 8 years of age and of the other at the time of his admission to the hospital. Hutchinson's teeth and the positive serologic reaction gave the proof of congenital syphilis. The grandmother's serum taken at that time showed a positive reaction. Her spinal fluid gave a positive Pandy reaction. The pupils were asymmetric and reacted sluggishly to light. With syphilitic therapy the Wassermann reaction of all 3 persons became negative and the mother's headache and fatigue disappeared.

KAJDI, Baltimore.

Diseases of Blood, Heart and Blood Vessels and Spleen

OSSEOUS CHANGES IN COOLEY'S ANEMIA. G. SPILIOPULOS, Jahrb. f. Kinderh. **148**:329 (March) 1937.

The author denies that the osseous changes reported as occurring with Cooley's anemia, consisting of widening of the substantia spongiosa with corresponding thinning of the cortex, osteoporosis and the appearance of furrows, is specific for this disease.

He states that identical changes may be found in the presence of chronic malaria, kala-azar and syphilis, as well as in cases of alimentary anemia and familial hemolytic icterus.

The appearance of the osseous changes depends on the age of the child at the beginning of the disease, the time of onset, the severity of the illness and the general condition of the child.

LANDAU, Hannibal, Mo.

CARDIOVASCULAR DISTURBANCES CAUSED BY QUALITATIVE MALNUTRITION. AUGUST MEYER, Zentralbl. f. inn. Med. **60**:577 (July 29) 1939.

General malnutrition (insufficient caloric intake) causes a drop in blood pressure and bradycardia; insufficient intake of protein, edema and anasarca, and deficiency in vitamin B_1 causes cardiovascular disturbances. Furthermore, impairment of the heart muscle and derangements of the peripheral circulation are recorded. The edema and the elevated blood pressure indicate that the kidneys are involved too.

In 1 case of beriberi combined with symptoms of pellagra and in another of dry pellagra the epithelium of the renal tubules showed damage similar to that found in cases of nephrosis. Both patients died with clinical signs of pseudouremia; at postmortem examination a contracted kidney was found in both of these patients.

Rats receiving a diet lacking vitamin B_1 revealed damaged kidneys similar to those observed in both of the patients just mentioned.

The author assumes that chronic deficiency of vitamin B_1 frequently might be the cause of chronic nephritis, of hypertension and of malignant nephrosclerosis.

From reports by American authors it is concluded that there is a considerable shortage in vitamin B_1 intake in the United States. Consequently, diseases due to deficiency in vitamin B_1 might be encountered in this country.

ARON, Chicago.

EXPERIENCES WITH TRANSFUSION OF PLASMA-FREE ERYTHROCYTES. H. BEUMER, E. LOESCHKE and K. SCHWARTZER, Ztschr. f. Kinderh. **61**:632 (Feb. 17) 1940.

The authors advocate transfusion of erythrocytes, especially for anemia following loss of blood and for anemia characterized by destruction of red cells or by diminished erythropoiesis. The plasma of whole blood may in some instances burden the circulation and the metabolic mechanism. Since red cells represent only about half the volume of whole blood, fewer transfusions are necessary. The plasma can be used for other conditions and under certain circumstances may be conserved for future use.

SIEMSEN, Chicago.

PHYSIOLOGIC AND DIAGNOSTIC IMPORTANCE OF THE CHLORINE CONTENT OF THE RED BLOOD CORPUSCLES. Ö. KERPEL-FRONIUS, Orvosi hetil. **83**:4388 (May 6) 1939.

Although the tissues of infants are rich in chlorine, the red blood cells are not more abundant than in older persons. Diminution of the chlorine content of the erythrocytes is without doubt a sign of salt deficiency. Normal or even high chlorine content of the red blood cells can be observed, however, in cases of great salt deficiency if the loss of water is greater than the loss of salt. Therefore the salt metabolism of the organism cannot be estimated from the chlorine content of the red blood cells.

GÖTTCHE, Budapest, Hungary.

CLINICAL PICTURE AND DIAGNOSIS OF OPEN DUCTUS OF BOTALLUS IN ADULTS. F. F. PIAYD, Vrach. delo **18**:625, 1935.

The author presents reports of 2 cases of open ductus arteriosus in adults with a complete discussion of the diagnosis and clinical picture of this anomaly.

One patient was a woman 21 years of age, presenting the characteristic clinical, physical and roentgen picture of the disease. The other was a 32 year old man, whose case is of special interest in that the diagnosis was confirmed by postmortem examination. In this case retarded physical development, pallor and dyspnea on exertion had been present since early childhood. Although the patient had been able to work as a carpenter and was even in military service for a time, he was never capable of systematic effort, and he became an invalid in the later years. Physical examination revealed a normal stature in the presence of malnutrition and poor muscle tone, as well as cyanosis of the lips, of the tips of the nose and of the ends of the fingers and toes and carotid pulsation. Examination of the heart revealed Gerhardt's area of dulness, together with a systolic thrill and a double murmur over the same area, a diastolic murmur over the aortic area and a transmission of the systolic murmur into the vessels of the neck on the left side. A distinct second pulmonic sound was observed, together with a rapid pulse, a capillary pulsation in the nails and a blood pressure of 135 systolic and 45 diastolic, as well as cardiac enlargement both to the right and to the left. Before death remittent fever and splenic enlargement developed. The antemortem diagnosis was subchronic septic endocarditis and patent ductus arteriosus. The anatomic diagnosis was as follows: acute ulcerative endocarditis of the aorta, persistent ductus botalli, dilatation, hypertrophy and myocardial degeneration and acute glomerulonephritis.

The author carefully analyzes the symptoms and cardiac signs of this anomaly, with special reference to diagnosis and differential diagnosis. An extensive review of the literature is presented.

BODER, Los Angeles.

VENOUS BLOOD PRESSURE FOLLOWING EXERCISE: A CRITERION OF THE CIRCULATORY FUNCTION. C. L. C. VAN NIEWENHUIZEN, Acta med. Scandinav. **103**:170, 1940.

The direct venous pressure is measured before and after a specified exercise at various intervals for ten minutes. The rise in pressure lasts less than thirty seconds in normal persons; after this period the venous pressure of healthy young persons becomes even lower than it was in the resting state and remains so for the rest of the observation period. Persons with slight evidences of decompensation have increased blood pressure from three to five minutes after exercise. With marked decompensation even the resting venous pressure is high, and the rise following exercise persists for the whole observation period.

KAJDI, Baltimore.

Diseases of the Nose, Throat and Ear

THE ROENTGEN DIAGNOSIS AND THERAPY OF RETROPHARYNGEAL ADENITIS. R. RHETT RATHBONE, Am. J. Roentgenol. **43**:25 (Jan.) 1940.

A series of lateral roentgenograms of 80 healthy children taken during inspiration were examined, and it was found that the normal retropharyngeal space in infants and children should not measure over 11 mm. by ordinary roentgen distances. Retropharyngeal adenitis was diagnosed in 20 instances on the basis of enlargement of the retropharyngeal space. This condition was usually due to some focal infection in the upper respiratory tract, often the nasal accessory sinuses. Of the 20 patients, 17 were treated with roentgen therapy, with complete disappearance of the retropharyngeal swelling in all cases. Both the area of swelling and the focus of infection should be treated by roentgen therapy.

SQUIRE, Chicago.

RELATION OF ENDOCRINE DYSFUNCTION TO OTOLARYNGOLOGY. CLAUDE C. CODY JR., Arch. Otolaryng. **30**:1 (July) 1939.

The author discusses the dual relation between endocrine dysfunction and otolaryngeal disease, concluding that foci of infection in the tonsils and paranasal sinuses may cause dysfunction of the thyroid, the pituitary body and the parathyroids and depress the action of insulin, with systemic consequences, and that a dysfunction of any of the three can produce a pathologic condition in the nose, larynx and ear.

GREENWOOD, Chicago.

DEFECTIVE SPEECH IN RELATION TO DEFECTIVE HEARING. MAX A. GOLDSTEIN, Arch. Otolaryng. **31**:38 (Jan.) 1940.

The dependence of perfect speech on perfect hearing, correct voice production, understanding of pitch, volume and rhythm and careful articulation is discussed. Various disorders of speech in childhood etiologically associated with defective hearing are presented. The importance of early cooperation with the otolaryngologist is emphasized.

GREENWOOD, Chicago.

RELATION OF ALLERGY AND TONSILLECTOMY IN CHILDREN: INCIDENCE OF RESPIRATORY ALLERGY IN CASES OF ROUTINE TONSILLECTOMY. FRENCH K. HANSEL and C. S. CHANG, Arch. Otolaryng. **31**:45 (Jan.) 1940.

The possibility of allergy as an etiologic factor must always be considered in controlling sinusitis, bronchitis, frequent colds and recurrent pneumonia. A physical examination, an adequate history and a complete cytologic study of the nasal secretion are essential in each case of suspected respiratory allergy in order that oversight may be avoided. It is pointed out that removal of tonsils and adenoids

does not always alleviate allergic symptoms, although, as a result of extensive study, the author observed that removal of tonsils and adenoids favorably influenced the incidence of head colds. Contrarily, an increase in pneumonia and bronchitis was noted.

GREENWOOD, Chicago.

VASCULAR FIBROMA OF THE NASOPHARYNX (NASOPHARYNGEAL FIBROMA). STANTON A. FRIEDBERG, Arch. Otolaryng. **31**:313 (Feb.) 1940.

The author presents 3 cases of "vascular fibroma," or "angiofibroma," in which treatment by irradiation and surgical diathermy was successfully employed. A definite decrease in the vascularity of irradiated areas was noted in 2 of the cases, despite the absence of histologic changes following irradiation. Uncontrollable hemorrhage resulted when no irradiation had been used. Avulsion with the cold snare is discouraged because of the attachment of the tumor to the bones of the base of the skull and the involvement of these bones by pressure necrosis.

GREENWOOD, Chicago.

RECURRENCE OF OTITIC INFECTIONS DUE TO THE BETA-HEMOLYTIC STREPTOCOCCUS. JOHN MARQUIS CONVERSE, J. A. M. A. **113**:1383 (Oct. 7) 1939.

The author presents cases of aural infection in which treatment with sulfanilamide was given and recurrences developed. In the first group, 4 cases, suppuration of the ear developed not long after cessation of sulfanilamide treatment for draining otitis due to the hemolytic streptococcus. The patients in these cases were relieved by adequate and longer courses of treatment with or without paracentesis and mastoidectomy. In the second group, 3 cases, meningitis developed three to four weeks after apparent recovery resulting from drainage, mastoidectomy and administration of sulfanilamide. This condition was treated as the symptoms demanded and with sufficient sulfanilamide to maintain a high level in the blood.

These cases led the author to feel that sulfanilamide should be given until not only clinical but bacteriologic cure is obtained. Many patients have insufficient antibody to combat the remaining organisms. He advises that sulfanilamide be used only in the treatment of severe and spreading infections and not in that of minor disorders, because of its masking effect, the chance of recurrence and the inadequacy of uncontrolled dosage. He infers that the use of the drug may inhibit antibody formation.

HEERSMA, Kalamazoo, Mich.

PREVENTION OF PURULENT OTITIS MEDIA IN INFANTS. HARRY BAKWIN and HAROLD JACOBZINER, J. Pediat. **14**:730 (June) 1939.

During the years from 1934 to 1938 the management of otitis media in infants under 2 years of age in the children's medical service of Bellevue Hospital was carefully supervised, and the following indications for myringotomy were set up: complete obliteration of the landmarks, especially of the short process, and a bulging gray drum, together with fever, restlessness and disturbed sleep. In the presence of intense pain, great restlessness and loss of sleep these criteria were modified. Frequent examinations were discouraged, because of the danger of transmission of added infection from the examiner to the patient and because it was felt that manipulation in the canal, by traumatizing an already inflamed drum, might aggravate the condition. All infants were examined while lying on the abdomen with the head turned away from the examiner. Myringotomy was performed only with the approval of an attending physician.

The incidence of purulent otitis media during the years from 1934 to 1938 was compared with that during a control period (1931 to 1933). During the control period the incidence was 23.3 per cent of all patients admitted, whereas from 1934 to 1938 it was reduced to 8.9 per cent. During the control period 1.8 times as many infants had bilateral purulent otitis media as had the unilateral condition;

in the period of supervision the patients with the unilateral condition outnumbered those with the bilateral. The incidence of purulent otitis media among the infants with diarrheal diseases and with pneumonia decreased to less than one third during the period of supervision. The number of infants operated on for disease of the mastoid was reduced from 1.38 per cent of all ward patients admitted during the control period to 0.56 per cent for the period of supervised management.

RAUH, Cincinnati.

A THYRATRON INFLECTOR, ITS BEHAVIOR WITH CERTAIN VOWELS AND ITS USE IN INSTRUCTING DEAF CHILDREN. TIKVAH ALPER STERNE and H. J. ZIMMERMAN, Laryngoscope **49**:708 (Aug.) 1939.

Sterne and Zimmerman describe the construction and use of a thyratron inflector to assist in the instruction of deaf children in voice production and control. The apparatus has a vertical row of lights arranged to flash in accordance with the fundamental pitch of the voice—the higher the pitch, the greater the number of lights which respond. Voice and the inflection of the voice are thus translated into visual symbols, to the great benefit of the deaf child, who ordinarily, being unable to hear his own voice, frequently pitches it badly and has to rely on his kinesthetic sensations for the determination of pitch.

The authors review the history of education of the deaf by instruments which translate sound into light impulses; they analyze the characteristics of vowel sounds, and review the theories of vowel production and relation of pitch to vowel sounds. The construction of the inflection indicator is described as an adaptation of Hunt's electronic frequency meter circuit with thyratrons. Included are an output meter to indicate the intensity of the voice and a loud speaker to enable the child to feel the vibrations due to a sound while he is watching the lights.

Sterne found that correct inflection in words and phrases cannot be taught until the child is able to place any speech sound at any desired pitch. The child is shown how to keep a certain number of lamps glowing steadily while a sound is being phonated; he then practices until he is able to do it. The children, guided partly by the tactile sensations from their fingers on the loudspeaker, develop kinesthetic memory for the pitch that causes any lamp to glow. Practice is given in phonating the vowels at specific pitch levels.

It is advised that young deaf children be trained with the inflection indicator to learn at an early age to inflect their voices within the narrow range used in ordinary speech.

WOOD, Newark, N. J. [ARCH. OTOLARYNG.]

THE EXPERIMENTAL PRODUCTION OF DEAFNESS IN YOUNG ANIMALS BY DIET. EDWARD MELLANBY, Laryngoscope **49**:1090 (Nov.) 1939.

Mellanby produced in young dogs by an experimental diet a pathologic condition of the labyrinthine capsule, both of the nerve supply and of the bone itself. The diet was deficient in vitamin A and carotene; it included much cereal and all other food values.

Litters of puppies 7 to 10 weeks old were started on the experimental diet deficient in vitamin A. Usually the behavior of the animals became abnormal after two to four months of such feeding, with great changes after four months. The dietetic periods were from four to ten months. A total of 51 labyrinths from 44 dogs were examined. Serial sections of 16 of these from 12 animals were cut, stained and examined. The histologic technic of the Ferens Institute for the Study of Otology was used with modifications. Apart from the specific effects produced by the vitamin A deficiency the health of the animals was usually fairly good, with steady gain in weight. Mellanby gives, as follows, the most obvious pathologic changes found in the labyrinths of these young dogs: " *a.* nerve degeneration, more especially of the cochlear neurons; *b,* new bony growth in the modiolus; *c.* overgrowth of the internal periosteal layer of the capsule; *d.* serous

labyrinthitis; *e.* degenerative changes of the organ of Corti and sensory epithelium of the semicircular canals." The new bone laid down was of periosteal origin and appeared constantly in two places, (1) in or near the modiolus and (2) around the internal auditory meatus. This new bone pressed on and elongated the nerves as they left the cochlea and vestibule. The degeneration of the eighth nerve, especially the cochlear neurones, appeared to be due to mechanical interference produced by bony overgrowth. Where bony overgrowth and nerve degeneration were advanced, serous labyrinthitis was always found.

WOOD, Newark, N. J. [ARCH. OTOLARYNG.]

INFLAMMATORY DISEASES OF THE UPPER PORTION OF THE RESPIRATORY TRACT. G. HALLORAN, M. J. Australia **1**:182 (Feb. 10) 1940.

Nasal obstruction is a preliminary factor in inflammatory diseases of the nose and sinuses. The author considers whether the white Australian is not already developing a typically narrow face in which nasal disorders are prone to develop. The possible influence of some tropical environment and the prevalence of sea bathing may also tend to increase sinal disease. Repeated head colds are undoubtedly the commonest cause of chronic sinusitis.

Antrums are present at birth, but the ethmoids must also be considered possible foci of infection. In diagnosis, transillumination must not be relied on. Diagnostic puncture and roentgen examination offer the most effective means of diagnosis.

In treatment, ventilation of the nose is essential. For chronic sinusitis radical operation is not advocated, but puncture of the antrum is frequently used.

Infection of tonsils and adenoids undoubtedly accompanies chronic sinusitis, but removal of these structures does not always hasten recovery.

There is apparently no definite relation between sinal infection and mental disease. There is definite relation between infected tonsils and cultures persistently yielding the streptococcus.

TENNEY, Madison, Wis.

THE ASCERTAINMENT OF DEAFNESS AND EAR DISEASE IN CHILDREN. T. C. LONIE, Proc. Roy. Soc. Med. **32**:1632 (Oct.) 1939.

"(1) The usual statistical returns of ear disease in school children are so variable that they cannot be regarded as indicating the prevalence of ear disease with anything approaching accuracy.

"(2) All *ad hoc* investigations, whether by means of the audiometer or otherwise, make it clear that much 'middle ear' disease is missed in the course of the routine examination of school children.

"(3) While there is a great need for a uniform method of examining hearing, something simpler than the audiometer is required so that the necessary test may be carried out at routine examinations.

"(4) Whatever the test it is virtually impossible to eliminate psychological factors in the child as a possible source of error."

AUTHOR'S SUMMARY.

Diseases of Lungs, Pleura and Mediastinum

OCCURRENCE, CLINICAL CHARACTERISTICS AND THERAPY OF PNEUMOCOCCUS XXXIII PNEUMONIA. A. DAVIDSON and J. G. M. BULLOWA, J. Infect. Dis. **66**:178 (March-April) 1940.

The authors compared their cases of pneumonia caused by pneumococcus type IX and pneumococcus type XXXIII as they occurred during 1938-1939 and state that the differentiation between the two types of pneumonia cannot be made clinically but can be done by immunologic methods.

TOOMEY, Cleveland.

ANOMALIES OF THE LUNGS WITH SPECIAL REFERENCE TO THE DANGER OF ABNORMAL VESSELS IN LOBECTOMY. H. A. HARRIS and IVOR LEWIS, J. Thoracic Surg. **9**:666 (Sept.) 1940.

The authors report a case of profuse arterial hemorrhage during lobectomy (lower lobe of the left lung) for bronchiectasis in a girl aged 5 years. Postmortem examination disclosed that an artery the size of the celiac axis, arising 2 cm. above the left side of the diaphragm and entering the left pulmonary lobe at a level corresponding to the free edge of the pulmonary ligament, had been cut.

The authors urge that all anomalies of the chest be carefully recorded. They point out that Evans and Thoma emphasized the importance of regarding the vascular system of the early embryo as a capillary plexus which grows in all directions. Subsequently, certain channels in the primitive capillary plexus enlarge and give rise to the named arteries and veins of the older embryo, the fetus and the child. Many parts of the capillary plexus may persist or disappear, and it is the normal range of variation in these processes which accounts for most of the anomalies.

The anomalous pulmonary arteries fall into two groups. They are either persistent enlargements of the embryonic capillary plexuses between the subclavian (fourth aortic arch) and the pulmonary artery (sixth aortic arch) or between the abdominal aorta and celiac axis and the pulmonary artery.

Anomalies of the pulmonary veins will consist of those persistent communications between the superior vena cava and the pulmonary veins and the inferior vena cava and these vessels, because of the embryonic relation of the lung bud to the primitive foregut.

Much remains to be learned about the bronchial vascular system.

DORSEY, Chicago.

PNEUMONIA IN INFANTS AND CHILDREN. CARROLL M. POUNDERS and F. M. KING, South. M. J. **33**:58 (Jan.) 1940.

The authors report as follows: "The pneumonias of infants and children are not so easily classified bacteriologically as are those of adults, and the unsatisfactory clinical division into lobar and bronchopneumonias is still used.

"The incidence and mortality rates are both high during the first two years. Bronchopneumonia is the usual variety seen during this time. . . .

"Good general care, including rest, relief from cough and other disturbing factors, fresh air, diet, fluids and oxygen, continues to be of the greatest importance despite the discovery of specific therapeutic agents. . . .

"Sulfapyridine appears to be as applicable to pneumococcus infections in infants and children as it is in those of adults and shows promise of satisfactorily reducing the death rate."

F. W. SCHULTZ, Chicago.

AGENESIS OF THE LUNG: THE REPORT OF A CASE. H. L. STOKES and C. J. O. BROWN, M. J. Australia **1**:49 (Jan. 13) 1940.

The authors report a case of congenital absence or aplasia of the lung discovered in a girl aged 12 years and 10 months, who had been referred to one of them for examination. Although in only a few cases so far has the diagnosis been made during life and proved at autopsy, there should be no difficulty in recognizing the condition if the possibility of its occurrence is borne in mind. Other conditions may present a similar clinical and roentgen picture, but tomograms, bronchoscopic examination and bronchograms made after the use of iodized poppy-seed oil should make an accurate differential diagnosis possible in all cases.

GONCE, Madison, Wis.

PNEUMONIA WITH PRIMARY INVOLVEMENT OF LYMPH NODES. SEBASTIAN PINELES, Bull. Soc. de pédiat. de Iasi **10**:7, 1939.

Two cases of pneumonia in children are reported, in which the first roentgen findings were interpreted as due to enlarged tracheobronchial lymph nodes. The author discusses the theories of development of the pneumonia in such cases.

LESLIE, Evanston, Ill.

SULFAPYRIDINE IN TREATMENT OF BRONCHOPNEUMONIA IN INFANTS. LUIGI ZINI and F. ARISI, Pediatria **47**:696 (Aug.) 1939.

Sulfapyridine was given to 25 children suffering from bronchopneumonia. There was a rapid fall in temperature, usually in twenty-four hours and in forty-eight hours at the most. There were rapid improvement in the general condition and resolution of the bronchopneumonia. The drug was well tolerated by the smallest infants and by premature babies. It was stopped on the fourth or fifth day. The dosage employed, according to age, was as follows:

Up to 6 months, 0.5 to 0.75 Gm. per day; 6 months to 2 years, 1 Gm. per day; 2 to 3 years, 1.25 Gm. per day; 3 to 7 years, 1.5 Gm. per day.

No toxic symptoms were noted. All the children recovered.

MARTOCCIO, Utica, N. Y.

TREATMENT OF THE PNEUMONIAS IN INFANCY. JOSE M. VALDES and PEDRO DEPETRIS, An. Soc. puericult. Buenos Aires **5**:192 (July-Sept.) 1938.

The authors present a very thorough paper on the treatment of the pneumonias in infancy. They include comments on serotherapy, vaccines and foreign proteins, sulfanilamide, transfusions for the anemia and shock, nutritive requirements, oxygen therapy, pneumothorax and symptomatic treatment. HERRON, Oak Ridge, La.

TRIANGULAR CARDIOPHRENIC SHADOWS IN INFANCY. J. R. ABDALA, J. S. SALABERRY and J. C. PELLERANO, Arch. argent. de pediat. **11**:186 (Feb.) 1939.

The triangular cardiophrenic shadows are relatively frequently encountered in early childhood. The authors report the finding of such shadows in 20 cases in one year.

The shadows may be equally frequent on the right and on the left side or may occur bilaterally. The shadows may be present without much modification for a long period. The presence of the condition responsible is accompanied by variable clinical symptoms. In some cases the shadows are transitory and reappear only with the recrudescence of the underlying causative disorder.

Bronchial pulmonary disorders are commonly present in the form of congestions or consolidations. Many times the condition is probably due to pulmonary atelectasis. Tuberculin reactions are almost always negative.

The authors believe that tuberculosis plays a minor role in the pathogenesis of this disorder. They believe that early postural drainage is probably the best measure to prevent bronchial dilatations.

SCHLUTZ, Chicago.

PNEUMOTHORAX AND SPONTANEOUS EMPYEMA IN THE YOUNG CHILD. A. ARIZTIA, Rev. chilena de pediat. **10**:1 (Jan.) 1939.

The author reports several cases of pyopneumothorax. In general he advises conservative treatment and thoracocentesis. Only for very severe involvement should thoracoplasty or rib resection be done.

The younger the child the more favorable will be the result with conservative treatment and avoidance of rib resection. Repeated blood transfusions are recommended.

SCHLUTZ, Chicago.

TRANSITORY PULMONARY CONDENSATIONS IN INFANTILE ASTHMA. A. ARIZTIA, Rev. chilena de pediat. **10**:521 (Sept.) 1939.

The author reports several cases of asthmatic children in whom roentgen examination showed transitory pulmonary condensation during the asthmatic attack. The condition was absent during the interval between attacks.

In the absence of a proved tuberculous or pneumonic process, such condensations when they occur without fever in a child whose general condition is good are transitory, have a good prognosis and are probably due to an allergic effect.

SCHLUTZ, Chicago.

IDIOPATHIC CHYLOTHORAX AND CHYLOUS ASCITES IN CHILDREN. ALOIS BOSSARD, Jahrb. f. Kinderh. **148**:258 (Feb.) 1937.

A 1½ year old girl was seen with double-sided chylothorax of undetermined causation, which healed after many punctures. The child later had flaccid paralysis of the legs, with sensory disturbances and incontinence of urine and stools. No clinical cause for this paraplegia could be found. Observation two and three-fourths years and seven and one-third years later revealed no residual signs of the chylothorax.

A girl of 11 months was seen with chylous ascites. Drainage was done twice, with the removal of considerable quantities of fluid in both instances. The third time, oxygen was introduced into the peritoneal cavity. This was followed by healing. Months later the child died after an injury to the skull. Autopsy showed that ascites was not present. The cause for this disease in this child was not found.

The authors advocate further attempts at therapy of the type described.

Chylous ascites is classified according to three types: (1) primary idiopathic, (2) pseudochylous and (3) secondary (to lymphatic erosion).

LANDAU, Hannibal, Mo.

CROUPOUS PNEUMONIA IN CHILDREN: COURSE OF ILLNESS AND MEANS OF INFLUENCING IT (SEROTHERAPY AND CANTHARIDES BLISTER). GERHARD JOPPICH, Jahrb. f. Kinderh. **149**:1 (April) 1937.

The clinical picture of extreme intoxication occurring in the presence of croupous pneumonia is described. The adverse effects on the circulatory and nervous systems are stressed. An illustration showing the effect on the heart is given. The typhoid and meningeal forms are discussed in some detail.

Convalescent serum of the proper type has been used with success. Illustrative case reports are given.

Studies were made in many of these cases with the cantharides blister. The blister fluid is clear during the height of the fever, but at the time of the crisis it becomes cloudy because of the presence of polymorphonuclear cells. This reaction does not occur when antipyretics are given.

LANDAU, Hannibal, Mo.

FATE OF INFANTS WITH SPASTIC BRONCHITIS. B. KOHLER and H. MAI, Ztschr. f. Kinderh. **61**:481 (Dec. 22) 1939.

Reports regarding the relation between bronchial asthma in infants and bronchial asthma in older persons vary greatly. An important consideration is a follow-up over a sufficiently long period. The author reports that of 86 infants observed over a period of ten years 12 had true asthma. The probability of asthma later in life is apparently greater in cases in which there is a positive family history of allergy. In the authors' group 62 per cent of the patients had such a family history. In a control group the incidence was 22 per cent.

SIEMSEN, Chicago.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

NORMAL VARIATION IN THE GASTROINTESTINAL RESPONSE OF HEALTHY CHILDREN. ICIE G. MACY, LAWRENCE REYNOLDS, HELEN J. SOUDERS and MARY BATES OLSON, Am. J. Roentgenol. **43**:394 (March) 1940.

Passage of milk and water through the gastrointestinal tract was checked by: (1) barium sulfate meals, in water and in milk; (2) carmine markers, and (3) the rate of passage of food residue. The duodenal bulb filled immediately in all cases.

The average time required for emptying the stomach with a water–barium sulfate mixture was one and nine-tenths hours; with a milk–barium sulfate mixture it was three and one-tenth hours.

Milk stimulated considerably more tone and vigorous peristalsis with a churning effect in the stomach and a prolonged emptying time. It took about half an hour for the barium to pass through the jejunum.

SQUIRE, Chicago.

CONGENITAL OBSTRUCTION OF DUODENUM. ROBERT ELMAN, Ann. Surg. **112**:234 (Aug.) 1940.

The author describes 3 cases of duodenal obstruction in infancy, due to volvulus of the entire small intestine plus congenital (extrinsic) bands occluding the terminal portion of the duodenum and the upper portion of the jejunum. The defect seems to be a failure in the third stage of intestinal rotation, associated with an attachment of the terminal part of the ileum to the upper part of the jejunum in the upper left quadrant. Recovery followed in all 3 cases when the volvulus was untwisted and the extrinsic bands were cut.

The most important symptom is persistent bile-stained vomitus. Vomiting begins shortly after birth but in some cases is interrupted by periods during which all food is normally retained. During periods of obstruction visible gastric peristalsis may be seen passing from left to right. Roentgenologically, no dilated loops of intestine are seen but a dilated stomach and duodenum can often be identified. There is often dehydration, and attacks of prostration and listlessness may occur.

When the diagnosis is made, unless the signs promptly disappear, celiotomy is indicated. General anesthesia and an adequate incision are necessary. According to the author, much time is saved and unnecessary intraperitoneal trauma is avoided by prompt evisceration of the entire small intestine. The volvulus is untwisted and the obstruction bands severed. Gastroenterostomy is unnecessary and adds to the risk of operation.

BANTIN, Omaha.

CONGENITAL ABSENCE OF THE GALL BLADDER AND OBLITERATION OF THE EXTRAHEPATIC BILE DUCTS. FRED S. BRUCHSALER, Arch. Pediat. **56**:731 (Nov.) 1939.

A clinical and pathologic report is made of a case of congenital obstruction of the extrahepatic bile ducts and absence of the gallbladder, which is an extremely rare anomaly.

These malformations are believed to be caused by a developmental anomaly. The ducts, like the gallbladder, are hollow structures which undergo temporary obliteration of their lumens in the early fetal stage. These lumens are later reestablished and the normal organs formed, but an arrest in this obliterative stage may produce atresia of any portion of the extrahepatic system.

ORR, Buffalo.

THE RAW APPLE DIET THERAPY OF DIARRHEA. A COMPARATIVE EVALUATION. ALFRED KERSHBAUM, Arch. Pediat. **57**:43 (Jan.) 1940.

Raw apple diet was found in 20 cases to be more effective in the treatment of diarrhea in children than any of the older methods of treatment.

ORR, Buffalo.

VITAMIN A ABSORPTION IN CELIAC DISEASE. B. B. BREESE JR. and AUGUSTA B. MCCOORD, J. Pediat. **15**:183 (Aug.) 1939.

Breese and McCoord report observations on the absorption of vitamin A from the intestines of 10 patients with celiac disease, of 1 with signs suggestive of cystic fibrosis of the pancreas and of 48 with other complaints. The procedure used for testing the absorption of vitamin A was that of Chesney and McCoord. After a basal blood specimen had been taken, the child was given orally an amount of fish liver oil which furnished 7,000 U. S. P. units per kilogram of body weight. Blood for determination of the vitamin A content was drawn two, four, six, nine, twelve and twenty-four hours after the administration of the oil. During the test the child received his regular meals. The patients with celiac disease, even after treatment, were unable to absorb vitamin A normally and when given a large amount of vitamin A by mouth did not show an increase in the vitamin A level in the blood equal to that of a group of children with other diseases. This inability to absorb vitamin A was more marked in patients with cystic fibrosis of the pancreas than in those with celiac disease.

RAUH, Cincinnati.

ACUTE APPENDICITIS IN CHILDHOOD: A STATISTICAL STUDY OF 848 CASES FROM THE CHILDREN'S HOSPITAL, BOSTON. HENRY W. HUDSON JR. and JOHN W. CHAMBERLAIN, J. Pediat. **15**:408 (Sept.) 1939.

A statistical study of 848 cases of acute appendicitis observed over a period of ten years is presented. A correlation of appendicitis with infection of the respiratory tract was not demonstrated. Infestation with Oxyuris vermicularis as a cause of acute inflammation of the appendix was infrequent, but such infestation may cause a clinical syndrome indistinguishable from appendicitis. No definite evidence was found that fecal concretions initiated the inflammation. In 92 per cent of the cases the white blood cell count was above 10,000 per cubic millimeter, and an increase in the polymorphonuclear cell count was present in 95 per cent of the cases. The classic triad of symptoms, abdominal pain, vomiting and slight fever, must be considered presumptive evidence of acute appendicitis. Together with these symptoms, careful and frequent examinations during the first twelve hours of illness will establish the diagnosis before perforation occurs. The method of treatment used at the Children's Hospital is outlined, and the mortality statistics are reported.

RAUH, Cincinnati.

PERITONEOSCOPY. C. DOUGLAS SAWYER, New York State J. Med. **39**:2022 (Nov. 1) 1939.

By means or the peritoneoscope it is possible to secure endoscopic inspection of the peritoneal cavity. In 1935 there was but one such instrument in use in the United States; at present one hundred and forty-eight peritoneoscopes are distributed about the country. The operation is a simple procedure, done generally with the region under local anesthesia, and has a distinct economic advantage over exploratory laparotomy. It may be of assistance in the diagnosis of hepatic cirrhosis, ascites, abdominal tumors, tuberculous peritonitis, peritoneal carcinomatosis, ectopic pregnancy and the operability of carcinoma of the stomach. By means of the peritoneoscope, material for biopsy may be taken under direct vision.

AIKMAN, Rochester, N. Y.

INFLUENCE OF INGESTION OF PANCREATIC JUICE UPON LIVER FAT IN DEPANCREATIZED DOG MAINTAINED WITH INSULIN. M. L. MONTGOMERY, C. ENTENMAN, G. E. GIBBS and I. L. CHAIKOFF, Proc. Soc. Exper. Biol. & Med. **43**:349 (Feb.) 1940.

These workers found that they were able to prevent the formation of fatty livers in depancreatized dogs maintained with insulin by feeding the external

secretions of the pancreas to these animals. Their findings are in contrast to the contention of Dragstedt and his associates (*Am. J. Physiol.* **117**:175, 1936) that the factor in the pancreas which inhibits the deposit of fat in the liver in depancreatized animals is unrelated to the external secretion of the pancreas.

HANSEN, Minneapolis.

EFFECT OF MEAT EXTRACT ON FATTY INFILTRATION OF LIVER IN DEPANCREATIZED AND DUCT-LIGATED DOGS. E. P. RALLI and S. H. RUBIN, Proc. Soc. Exper. Biol. & Med. **43**:601 (April) 1940.

The hepatic lipids in depancreatized dogs and in dogs with the pancreatic ducts ligated were not increased when meat powder (the extractives had been removed) was fed to the experimental animals, and this was in striking contrast to the results when meat was fed. When meat extract was added to the diet of 2 depancreatized dogs and to 1 dog with the ducts ligated the hepatic lipids were again greatly increased.

HANSEN, Minneapolis.

PRODUCTION OF GASTRIC AND DUODENAL ULCERS IN THE CAT BY THE INTRAMUSCULAR IMPLANTATION OF HISTAMINE. S. H. WALPOLE, R. L. VARCO, C. F. CODE and O. H. WANGENSTEEN, Proc. Soc. Exper. Biol. & Med. **44**:619 (June) 1940.

Seven cats were given repeated intramuscular injections of histamine in yellow wax U. S. P., which stimulated a copious flow of gastric juice containing free acid. In all animals erosion and ulceration of the stomach and of the duodenum were demonstrated on examination three to twenty-five days later, after having received 60 to 480 mg. of histamine. No ulcers were found in 13 control cats. The constant stimulation of gastric secretion with histamine in yellow wax gives a reaction entirely different from that observed when histamine is given in watery solution.

HANSEN, Minneapolis.

THE SERUM CHOLINE ESTERASE IN JAUNDICE AND DISEASES OF THE LIVER. BRIAN MCARDLE, Quart. J. Med. **9**:107 (Jan.) 1940.

McArdle measured the serum choline esterase in a group of 270 persons. He used the method of Jones and Tod, which consists of measuring in a Bancroft manometer the amount of carbon dioxide liberated when acetylcholine is added to a mixture of serum and Ringer's solution. The enzyme esterase breaks down the acetylcholine to choline and acetic acid, which reacts with the bicarbonate of the Ringer's solution to form carbon dioxide.

In 40 normal adults the range was from 51 to 121 units, with a mean of 78 units. For children (7 to 15 years old) the values varied from 71 to 166 units, the mean being 105 units.

With diseases of the liver the values were much lower. It is suggested that the determination of serum choline esterase might be employed both as a measure of hepatic function and as a test in differentiating jaundice of hepatic and obstructive origin. A value below 50 units indicates that the liver is damaged, according to the author.

BRADFORD, Rochester, N. Y.

STOMATITIS IN CHILDHOOD. CLIFFORD G. PARSONS, Arch. Dis. Childhood **15**:43 (March) 1940.

In a study of 115 cases of stomatitis, four fifths of the patients being under 3 years of age, it was found that, of the many forms of treatment, 1 per cent aqueous solution of gentian violet or tincture of merthiolate was the most effective.

KELLY, Milwaukee.

DIARRHEA IN INFANCY AND CHILDHOOD. H. B. BASU, Indian J. Pediat. **7**:80 (April) 1940.

Diarrhea is discussed under the following headings: dietetic, infective and parenteral.

The use of fluids parenterally is apparently less common in India than in the United States, as it is advised only for very toxic conditions.

TENNEY, Madison, Wis.

FURTHER OBSERVATIONS ON THE RELATION OF THE DECLINE IN THE NUMBER OF HORSE-DRAWN VEHICLES TO THE FALL IN THE SUMMER DIARRHOEA DEATH-RATE. G. S. GRAHAM-SMITH, J. Hyg. **39**:558 (Sept.) 1939.

During the past thirty-seven years the death rate from summer diarrhea in children under 1 year of age per thousand live births in England and Wales has declined from an average of 25.4 for the first five years (1901 through 1905) to 5.3 for the last five years (1933 through 1937). During the first twenty-one years the death rate showed great fluctuation, rises occurring in the hot months, but during the last sixteen years it has shown little fluctuation, suggesting that a high atmospheric temperature in the third quarter of the year is not in itself a cause of the disease.

In the last thirty years the number of horses kept in larger cities has decreased to about one thirtieth, and regulations preventing accumulation of horse manure and of refuse have been enforced, greatly reducing places suitable for breeding of flies.

The number of domestic flies has been greatly diminished, even though, aside from the presence of horses, conditions suitable for their growth have in several cities been favorable.

The author believes that this reduction in the number of horses and in the accumulation of horse manure, by decreasing the breeding places for flies, has been largely responsible for the diminished incidence of infantile diarrhea.

JANNEY, Wauwatosa, Wis.

MULTIPLE HEMANGIOMAS OF THE LIVER IN A PREMATURE INFANT. H. SLOBOZIANU and M. PAVLOVICI-GHINEA, Arch. de méd. d. enf. **43**:158 (May-June) 1940.

Occasional instances of simple or cavernous hemangiomas of the liver are found in extrauterine life, but, although more rarely, these tumors may appear in the intrauterine period or in the premature child. Adalid and Escaro have published (1932) an interesting observation on a newborn child who presented, on the third day, signs of internal hemorrhage. At operation a cavernous angioma was found in the left lobe of the enormously distended liver; this tumor had ruptured, and the hemorrhage was uncontrollable.

Since this report 11 further cases have been recorded, in some of which the tumors were single, and in others, multiple. The writers report the history and clinical findings concerning an infant of 3 days, together with a complete pathologic summary.

AMESSE, Denver.

CIRRHOSIS OF THE LIVER IN CHILDREN. P. BUONOCORE, Pediatria **47**:629 (Aug.) 1939.

The author sets out to determine the character of the cirrhotic process and to distinguish it from the various forms of chronic hepatitis. The origin of the concept of cirrhosis is discussed, and also the histologic limits. The histologic, anatomic and clinical differences between cirrhosis and chronic hepatitis are discussed. However, histologic data offer the best way of classifying the chronic diseases of the liver. Cirrhosis of the liver is very rare in children. From 1930 to 1938 6 cases were observed among 4,500 admissions to the author's clinic.

On 2 of the patients autopsies were done, and the histologic observations are listed. The total number of autopsies in the clinic for this period was 625. A complete description of the 6 cases is given. The youngest patients were 4 years of age, and the oldest were 11 years old. Cirrhosis is characterized by its chronic course. Often the first symptoms are those of hepatic decompensation, and often the prodromal symptoms referable to the gastrointestinal tract are lacking. There is a long latent period before the symptoms appear. Ascites is the most constant symptom and almost always the first to call attention to the disease. Often the ascites is accompanied with jaundice and even fever. Jaundice is more frequent in the hypertrophic form. Epistaxis, bleeding gums and generalized purpura frequently are present. Death often occurs in coma or by intercurrent infection.

MARTOCCIO, Utica, N. Y.

TREATMENT OF SEVERE ALIMENTARY INTOXICATION IN INFANTS. E. A. VOSS, Kinderärztl. Praxis **10**:393 (Sept.) 1939.

The treatment in use at the Heidelberg University Children's Hospital is described. Saline solution is given subcutaneously and 50 cc. of dextrose solution from three to four times daily, intravenously. No mention is made of administration of fluids by continuous intravenous drip. The starvation period is prolonged to six or seven days; tea is given by mouth. After an initial gastric lavage, high enemas are given while the infant is placed in a hot bath. To eliminate all remnants of previous feedings, this treatment may have to be repeated daily for a few days. Feeding is started with skimmed breast milk in small amounts; this milk is believed to be superior even to buttermilk. Casein or protein milk is not mentioned.

HEYMANN, Cleveland.

DIFFERENT FORMS OF INTESTINAL GRIPPE IN EARLY CHILDHOOD. J. DUKEN, Kinderärztl. Praxis **10**:449 (Oct.) 1939.

Intestinal grip in older children is characterized by hematemesis, tachycardia with extrasystole and arrhythmia, blood in the stools, with or without diarrhea, and enlargement of the liver.

In infants the predominant sign is loss in weight, which in the first days is not sufficiently explained by vomiting or diarrhea. Diarrhea develops later, and the stools are mixed with pus and mucus. In spite of correct treatment the loss in weight often continues and leads to decomposition rather than to intoxication. The temperature is only slightly elevated. The mortality rate is 55 per cent. A diet of skimmed breast milk gave the best results in the cases described.

HEYMANN, Cleveland.

Nervous Diseases

SODIUM DIPHENYL HYDANTOINATE IN TREATMENT OF CONVULSIVE SEIZURES: TOXIC SYMPTOMS AND THEIR PREVENTION. H. HOUSTON MERRITT and TRACY J. PUTNAM, Arch. Neurol. & Psychiat. **42**:1053 (Dec.) 1939.

The authors express the belief that sodium diphenyl hydantoinate should be used in cases of convulsions not relieved by the other anticonvulsive drugs. The percentage of minor toxic reactions is greater than that encountered with the use of other drugs, such as phenobarbital.

BEVERLY, Chicago.

EXPERIMENTAL EVIDENCE OF ANTICONVULSANT PROPERTIES OF SODIUM DIPHENYL HYDANTOINATE (DILANTIN SODIUM N. N. R.). H. H. GOLDSTEIN and J. WEINBERG, Arch. Neurol. & Psychiat. **43**:453 (March) 1940.

The authors demonstrated the anticonvulsant properties of dilantin by the administration of metrazol subcutaneously to a group of epileptic patients before and after the giving of dilantin sodium N. N. R.

BEVERLY, Chicago.

PONTILE ABSCESS. JOSEPH B. GAIDA, Arch. Otolaryng. **30**:93 (July) 1939.

The author presents a case of pyogenic pontile abscess. Only 11 such cases have been previously reported in the literature. The clinical picture is discussed, and, as a particular point of interest, attention is called to simultaneous involvement of the right external and left internal rectus muscles. Paralysis of the lateral gaze denotes principally an intrapontile lesion. A lesion in the pons causes homolateral paralysis of the sixth nerve with contralateral paralysis of the nucleus of the internal rectus muscle.

GREENWOOD, Chicago.

CONVULSIONS IN THE CHRONIC NERVOUS DISEASES OF INFANCY AND CHILDHOOD. A REVIEW OF 1,660 CASES. ALBERT W. PIGOTT, SAMUEL M. WEINGROW and THOMAS S. P. FITCH, Arch. Pediat. **56**:703 (Nov.) 1939.

This is the first of a series of articles embracing a critical review of 1,660 cases of epilepsy. In this publication the authors have subdivided their cases according to etiologic factors.

ORR, Buffalo.

CONVULSIONS IN THE CHRONIC NERVOUS DISEASES OF INFANCY AND CHILDHOOD. ALBERT W. PIGOTT, SAMUEL M. WEINGROW and THOMAS S. P. FITCH, Arch. Pediat. **56**:781 (Dec.) 1939.

In the analysis of their material obtained from a study of 1,660 cases the authors have classified the auras presented by their patients into the various areas described previously by Penfield and others. Definite auras were present in 295 persons. In 492 cases auras either were definitely absent or it was impossible to ascertain their presence or absence because of mental deterioration, psychosis or aphasia.

In many instances the patient was too young to describe an aura if it was present. In 213 cases the presence or absence of an aura has not as yet been fully investigated.

ORR, Buffalo.

CONVULSIONS IN THE CHRONIC NERVOUS DISEASES OF INFANCY AND CHILDHOOD. ALBERT W. PIGOTT, SAMUEL M. WEINGROW and THOMAS S. P. FITCH, Arch. Pediat. **57**:12 (Jan.) 1940.

This is a continuation of a series of articles on this subject, in which the neurologic and encephalographic observations in 1,660 cases are described.

ORR, Buffalo.

TREATMENT OF PNEUMOCOCCI MENINGITIS WITH SULFAPYRIDINE AND THE SODIUM SALT OF SULFAPYRIDINE. HORACE L. HODES, HARRY S. GIMBEL and GEORGE W. BURNETT, J. A. M. A. **113**:1614 (Oct. 28) 1939.

Seventeen patients with pneumococcic meningitis were treated with sulfapyridine or with sulfapyridine and its soluble sodium salt. Four were infants and 5 children. Eight patients recovered completely, in contrast to 1 recovery among the 46 patients treated just previously.

The authors feel that a great advantage is gained by using the sodium salt intravenously.

The concentration of sulfapyridine in the blood and spinal fluid can be watched and maintained at a level of from 10 to 15 mg. per hundred cubic centimeters, and since the absorption is so variable the intravenous therapy may be optional.

Four patients (3 infants) died of the disease within twenty-four hours or from a complication. The reactions of hematuria and of granulocytopenia were not responsible

HEERSMA, Kalamazoo, Mich.

EPIDEMIC ENCEPHALITIS IN NORTH DAKOTA. PAUL J. BRESLICH, PAUL H. ROWE and WILLIAM J. LEHMAN, J. A. M. A. **113**:1722 (Nov. 4) 1939.

Of 23 patients with epidemic encephalitis 4 were children. There was sudden onset of high fever, with vomiting, nervous irritability and convulsions. There were coma and spasmodic twitching in 2 instances. The children had a shorter and more favorable course than did the adults. Five of the adult patients died. The epidemic was possibly related to a concurrent epidemic of equine encephalitis.

HEERSMA, Kalamazoo, Mich.

INFLUENZAL MENINGITIS. NELLES SILVERTHORNE, ALAN BROWN, W. M. JOHNSTONE and AGNES WALKER, J. Pediat. **16**:456 (April) 1940.

The treatment of 65 infants and children suffering from influenzal meningitis forms the basis of this study. During the period from 1919 to 1929, 70 patients with this disease were treated, with only 1 recovery. During the period from 1930 to 1939, 65 patients were treated and 15 recovered. The methods of treatment used in this series of cases are outlined. Little difference in the mortality rate was found with Fothergill's method (anti-influenzal horse serum given intravenously and anti-influenzal horse serum and human serum given intrathecally) and with the authors' method of using anti-influenzal horse serum intravenously and bactericidal guinea pig serum intrathecally. Bactericidal guinea pig serum is difficult to obtain and is impractical for widespread use. Efforts are now being made to develop an immune rabbit serum. Results with chemotherapy (sulfanilamide and sulfapyridine) have not been convincing enough to justify using these drugs alone. One recovery is reported with the use of sulfapyridine and immune rabbit serum. The method of production of immune rabbit serum and the technic of mouse protection tests to determine the presence of antibodies in the serum are described. The authors recommend the use of immune serum mixtures plus chemotherapeutic agents in the treatment of influenzal meningitis.

RAUH, Cincinnati.

TETANY IN INFANCY AND CHILDHOOD: A CLINICAL STUDY OF FORTY-FIVE CASES SEEN IN NORTH CHINA, WITH ESPECIAL REFERENCE TO ETIOLOGY. FU-T'ANG CHU and CHIEH SUNG, J. Pediat. **16**:607 (May) 1940.

Chu and Sung in a study of 45 cases of tetany in North China, found the conditions observed in these cases to differ in certain etiologic factors from those reported in the occidental literature. The onset of symptoms occurred before the age of 3 months in 66.7 per cent and before the age of 6 months in 82.2 per cent. Eighty per cent of the mothers of their patients showed impaired calcium metabolism during pregnancy and lactation. Many of the patients showed rickets during the first three months after birth. In 72.2 per cent of the cases there was visible roentgen evidence of rickets, most of which was mild. The younger the patient, the less likely were rachitic changes to be found in the roentgenogram. In 50 per cent of the cases the patients were breast fed before the development of tetany. If the mother's nutrition is not adequate, human milk should not be relied on to protect the infant from tetany.

RAUH, Cincinnati.

INFLUENZAL MENINGITIS TREATED WITH SULFAPYRIDINE—REPORT OF TWO CASES WITH RECOVERY. J. I. WARING, J. South Carolina M. A. **35**:284 (Nov.) 1939.

Eleven cases of influenzal meningitis are reported. Sulfapyridine was used for 5 of the patients, including the 2 who recovered, and sulfanilamide was used for 6. Nine of the patients died. Both of the patients who recovered were Negroes. The first was a girl aged 6 years and the second a boy aged 22 months. It is interesting to note that both of these children had residual symptoms. The girl remained deaf; this was not explained by examinations of the external or of the middle ear. The boy showed slight ataxia on discharge, two months later.

WESTON, Columbia, S. C.

THE GUILLAIN-BARRÉ SYNDROME. E. SUSMAN and K. MADDOX, M. J. Australia **1**:158 (Feb. 3) 1940.

The authors present detailed case histories of 7 cases of polyneuritis of unknown origin (neuronitis) and a general discussion of this syndrome.

GONCE, Madison, Wis.

INTRATHECAL ADMINISTRATION OF SULFANILAMIDE FOR PURULENT MENINGITIS. R. MARTIN, PANTHIER, MOUAILL and HAMOND, Presse méd. **48**:101 (Jan. 31-Feb. 3) 1940.

Sulfanilamide administered by mouth appears in the cerebrospinal fluid in nearly the same concentration as in the blood. Oral administration is the method of choice in the treatment of meningitis. Sulfanilamide given by the lumbar route will increase the concentration in the spinal fluid for six hours or more. In the treatment of pneumococcic meningitis, some advantage is gained by using sulfanilamide by intrathecal injection as well as by mouth. When serum is injected in treatment, sulfanilamide should be added to prevent any fall in the level in the spinal fluid.

DAFFINEE, Boston.

SPONGIOBLASTOMA INVADING THE THIRD VENTRICLE AND PRODUCING A PROGRESSIVE CACHEXIA. J. LHERMITTE, T. DE MARTEL, J. GUILLAUME and AJURIAGUERRA, Rev. neurol. **71**:166 (Feb.) 1939.

At the age of 5 years a girl previously in good health began to lose weight. Her condition did not become markedly worse until two years later, when frontal headache, vomiting and total lack of appetite produced cachexia. At the age of 8 her head became larger, and her intellect began to fail. She had periods of profound sleep. Her vision deteriorated. At that age she was first seen by the authors. Emaciation was extreme, and she seemed to be in a semistupor. The blood pressure was 80 systolic and 40 diastolic; the basal metabolic rate was —2 per cent. Neurologic examination revealed muscular hypotonia, weak deep reflexes and absent cutaneous reflexes. There was bilateral optic atrophy. Roentgenograms showed the presence of hydrocephalus. Simmonds' disease seemed the most likely diagnosis, but the condition of the child prohibited any operation except a bilateral ventricular puncture. The child died several days later. At autopsy the pituitary was found to be normal. A large infiltrating spongioblastoma was found in the subthalamic region.

DAFFINEE, Boston.

ENCEPHALITIS OF THE SYMPATHETIC CENTERS: A SYNDROME OF SOMNOLENCE, POLYPHAGIA, AND POLYDIPSIA. A. GORDON, Rev. neurol. **71**:411 (April) 1939.

The author presents 2 cases of a rare combination of symptoms, which he considers true examples of encephalitis involving the sympathetic centers.

DAFFINEE, Boston.

PROLONGED CHOREA. L. BABONNEIX and P. GUILLY, Rev. neurol. **72**:149 (Aug.) 1939.

Three cases are described in which chorea persisted over a longer period than usual. In all 3 cases there were abnormal neurologic signs and symptoms suggesting complicating lesions. Numerous cases previously reported by other authors are discussed. Babonneix and Guilly conclude that the diagnosis of prolonged chorea can be made only after eliminating conditions which do not produce persistent choreiform movements immediately following acute Sydenham chorea. They also point out that prolonged chorea may follow simple chorea because of psychic or organic causes.

DAFFINEE, Boston.

MACROGENITOSOMIA IN A CASE OF SCHILDER'S DISEASE. L. FIOZHAUT-ZELDOWICZ, Rev. neurol. **72**:188 (Aug.) 1939.

A boy of 7½ years had developed normally up to the age of 3 years. His penis had always been large and his stature above normal. Profound mental changes appeared during the third year of life. At the age of 7 years epileptic attacks appeared. The fasting value for blood sugar was 37 mg. per hundred cubic centimeters. Encephalograms revealed both external and internal hydrocephalus, with marked dilatation of the third ventricle. The author concludes that in addition to the diffuse cortical atrophy and the lesions in the basal ganglions there must be involvement of the sugar-regulating centers and the centers regulating genital growth.

DAFFINEE, Boston.

EFFECT OF EPINEPHRINE ON THE ELECTROCARDIOGRAM AS A MEANS OF EXAMINING THE NEUROVEGETATIVE SYSTEM. U. WIDMER, Med. ital. **20**:495 (Oct.) 1939.

The author briefly refers to the different methods of investigating the neurovegetative system. He discusses one based on the behavior of the electrocardiogram after injection of epinephrine. He studied 14 nursing infants, all under 11 months of age. He concludes that this method is not reliable for nursing infants and that it is not easy to apply.

MARTOCCIO, Utica, N. Y.

TWO CASES OF FAMILIAL MICROCEPHALY. E. COMOLLI, Med. ital. **20**:536 (Nov.) 1939.

The author gives the physical findings and laboratory data in 2 cases of microcephaly in the same family, the patients being a sister aged 5 years and a brother aged 3 years. The anthropometric measurements and the encephalograms are presented.

MARTOCCIO, Utica, N. Y.

SEASONAL VARIATIONS IN THE EXCITABILITY AND TONUS OF THE AUTONOMIC SYSTEM. P. MANFRINI, Med. ital. **20**:585 (Dec.) 1939.

The author studied the behavior of the oculocardiac reflex in children aged 6 to 12 years. He noted that the reflex was more strongly positive in the cold months, with the apex at the onset of spring, and that there was behavior analogous to that of neuromuscular hyperexcitability and of spasmophilic states. To elicit the reflex, pressure is made over the eyeballs. This causes slowing of the pulse, respiration, lowering of the arterial pressure and sometimes a feeling of nausea. The reflex is considered normal when the pulse is slowed from 5 to 10 beats per minute, positive when it slows more than 10 beats, absent when there is no slowing and reversed when there is acceleration instead of slowing. The children were observed for ten to twelve months. The abdominal-cardiac reflex (solar reflex) was found to be more positive in the warm months, with the apex in July and August. This reflex consists in an increase in the pulse rate and a diminution in the arterial pressure with the sudden change from the horizontal to the erect posture.

MARTOCCIO, Utica, N. Y.

A CASE OF ACUTE IDIOPATHIC SUBARACHNOID HEMORRHAGE. M. SACCA, Pediatria **47**:822 (Sept.) 1939.

Acute subarachnoid hemorrhage can be divided into two types, that secondary to a process that can injure the vessel walls (syphilis, arteriosclerosis, toxic and mechanical factors) and an idiopathic type. The author presents the case of a 10 year old child with sudden onset of vomiting and pain along the spinal column, nuchal rigidity and positive Kernig and Brudzinski signs. There was difficulty

in making the child sit up. The cranial nerves were not affected. The Babinski sign was negative. The temperature was 37 C. Lumbar puncture gave a bloody spinal fluid under increased pressure; centrifugation of this fluid showed it to be xanthochromic. The Wassermann reaction of the blood was negative. The author feels that subarachnoid hemorrhage must be considered in the differential diagnosis of all acute meningeal diseases.

MARTOCCIO, Utica, N. Y.

SPASMOPHILIA IN THE BREAST-FED INFANT SHOWING GENERAL HYPERTONICITY. J. R. MARCOS and A. MUNILLA, Arch. de pediat. d. Uruguay **10**:616 (Oct.) 1939.

The authors report the occurrence of this condition in an infant 7 months of age, nourished entirely at the breast. The condition was observed during a mild diarrheal attack, in the course of which severe coma and generalized hypertonicity developed. The infant was exclusively breast fed, had never been ill before and did not present any evidence of rickets.

The condition subsided rapidly with intravenous calcium therapy. The blood showed hypocalcemia, hyperphosphatemia and diminution of the alkaline reserve.

SCHLUTZ, Chicago.

TRANSMITTING POWER OF BARRIER BETWEEN BLOOD AND CEREBROSPINAL FLUID IN MENINGITIS. D. MÓRITZ and B. WOLLEK, Orvosi hetil. **83**:641 (July 1) 1939.

The authors made systematic investigations on children suffering from tuberculous meningitis. They determined fixed bases and the values for chlorine, organic acids, bicarbonates, phosphates and proteins, both in the cerebrospinal fluid and in the blood. The results showed that the diminution of the chlorine content is most marked and is greater in the cerebrospinal fluid than in the blood. The amount of organic acids is increased in the blood as well as in the cerebrospinal fluid, the increase in the latter being 3 times greater than that in the blood. That the organism may be able to maintain the acid-base equilibrium, the chlorine content has to be diminished. This diminution is made easier by an increased transmitting power of the barrier between the blood and the cerebrospinal fluid.

GÖTTCHE, Budapest, Hungary.

EARLY MORTALITY OF INFANTS AND HEMORRHAGE OF THE BRAIN. ARVO YLPPÖ, Orvosképzés **29**:427 (May) 1939.

It is well known that infant mortality is diminishing steadily in most European states; in Finland, for example, it was 6.7 per cent in 1935. On the other hand, the number of early deaths and of stillbirths, the so-called "perinatal mortality," has remained the same; this perinatal mortality is about half the whole infant mortality in Finland. The first step toward clearing up this important question is pathologic examination of infants who die early. Ylppö's pathologic examinations showed that the cause of death of newborn infants with a birth weight of 700 to 1,000 Gm. was hemorrhage of the brain or of the spinal cord in 90 per cent of the cases. Among newborn infants over this weight hemorrhages were rarer. If these hemorrhages are not so extensive that they threaten life they may become manifest later. According to Ylppö, the cause of the so-called "Little's disease" is also hemorrhage of the central nervous system. The origin of many other diseases of the nervous system (such as idiocy and in many cases microcephaly or hydrocephalus) is also to be sought in these hemorrhages. It is therefore easy to understand that the avoidance of miscarraiges is one of the greatest problems of obstetricians and of pediatricians.

GÖTTCHE, Budapest, Hungary.

Psychology and Psychiatry

INFANTILE MONGOLISM: I. SYPHILITIC KERATITIS IN A MONGOLOID GIRL AGED TEN MONTHS. M. PÉHU and ROBERT PERRIN, Rev. franç. de pédiat. **13**:209, 1937.

A case is reported. The authors think that syphilis and mongolism occurred coincidentally and were not causally related. LESLIE, Evanston, Ill.

INFANTILE MONGOLISM: II. FAMILIAL MONGOLISM, CONJUGAL SYPHILIS DEVELOPING AFTER THE BIRTH OF FOUR CHILDREN WITH MONGOLISM. M. PÉHU and J. GATÉ, Rev. franç. de pédiat. **13**:212, 1937.

Four cases of mongolism in one family are reported. Because of two late miscarriages, the mother was given energetic antisyphilitic treatment during the last pregnancy, which, nevertheless, resulted in the birth of a fourth child with mongolism. Furthermore, after this both father and mother had indisputable acquired syphilis. The authors feel that this observation lends a great deal of weight to the opinion that mongolism is in no way related to syphilis.

LESLIE, Evanston, Ill.

CRISIS OF CHILDHOOD OR CRISIS OF THE FAMILY? LUIS MORZONE, Bol. Inst. internac. am. de protec. a la infancia **14**:12 (July) 1940.

In this rather long article it is maintained that the disintegration of the family is largely responsible for the existence of a great number of children who present physical, sensorial, intellectual and moral deficiencies. Education should be directed toward building up the family and its cooperation with the schools.

LESLIE, Evanston, Ill.

THE ONTOGENESIS OF THE SMILE. J. BILLSTRÖM, Acta pædiat. **25**:28, 1939.

The observations and interpretations of divers writers are reviewed discursively. The tone of the paper is strongly philosophic. MCCUNE, New York.

Diseases of the Genitourinary Tract

CONCENTRATED HUMAN BLOOD SERUM AS A DIURETIC IN NEPHROSIS. C. ANDERSON ALDRICH and H. H. BOYLE, J. A. M. A. **114**:1062 (March 23) 1940.

Seven patients in addition to 9 previously reported on were given four times concentrated human blood serum for nephrosis. Apparently early administration produced a more beneficial effect than did late administration in reducing the edema and starting diuresis. The presence of hematuria indicating other renal pathologic conditions, the presence of infection and late administration were factors acting against successful serum therapy. Serum free of hemolysis produced no reactions. HEERSMA, Kalamazoo, Mich.

ACUTE NEPHRITIS IN CHILDHOOD, WITH SPECIAL REFERENCE TO THE DIAGNOSIS OF FOCAL NEPHRITIS. W. W. PAYNE and R. S. ILLINGWORTH, Quart. J. Med. **9**:37 (Jan.) 1940.

The authors present a clinical study of a group of 301 cases of nephritis in children seen in the acute stage and of 64 cases observed in subsequent stages of the disease. They set out to decide whether anything was to be gained by distinguishing the focal from the diffuse type of nephritis. They concluded that acute focal nephritis is not a clinical entity.

Using the criteria given by Volhard and Fahr, the authors divided their cases into three groups: (1) no edema, (2) no edema other than puffiness of the eyelids and (3) definite edema. No difference between the three groups could be found as regards etiologic factors, age, sex or causative infection. It was impossible in the majority of cases to estimate the duration of the interval between infection and nephritis. The edematous condition commenced at the height of the infection quite as frequently as did the nonedematous. There was no difference in the frequency with which nitrogen retention occurred. Hypertension and oliguria were of no value in distinguishing the two types of nephritis. The prognosis in the three groups was equally serious. The authors concluded that the presence of edema as well as other criteria is useless for the distinction of focal from diffuse nephritis.

BRADFORD, Rochester, N. Y.

MANDELIC ACID IN TREATMENT OF PYURIA IN CHILDREN. J. GELDRICH and P. DUDÁS, Orvosi hetil. **83**:935 (Oct. 14) 1939.

The effect of mandelic acid is based on the fact that it is a fairly strong acid and passes through the kidneys unchanged, thereby producing a strong bactericidal effect. Its curative result needs two conditions: (1) that the mandelic acid should have a high concentration in the urine (0.25 to 0.5 per cent), and (2) that the hydrogen ion concentration of the urine should be about 5. Mandelic acid is most effective in cases of pyuria caused by coli bacilli (of 30 patients, 23 recovered and 6 improved), whereas pyuria caused by different cocci can be treated more successfully with sulfanilamide preparations.

GÖTTCHE, Budapest, Hungary.

HYPNOTIC TREATMENT OF ENURESIS NOCTURNA. J. BILLSTRÖM, Acta pædiat. **26**:62, 1939.

In skilled hands hypnosis is sometimes a valuable adjunct to the treatment of bedwetting.

McCUNE, New York.

A SUCCESSFUL OPERATIVE TREATMENT OF HYPERNEPHROMA IN A 1½ YEAR OLD CHILD. P. HELLSTRÖM, Acta pædiat. **26**:217, 1939.

The combination of roentgen treatment (1,800 r) with surgical extirpation of the tumor resulted in the survival of the patient, who was examined and found to be in good physical condition three months after operation.

McCUNE, New York.

Diseases of the Ductless Glands; Endocrinology

EXPERIMENTAL GOITER DUE TO CALCIUM. C. ALEXANDER HELLWIG, Arch. Surg. **40**:98 (Jan.) 1940.

Until recently, endemic goiter was regarded as a deficiency disease due to lack of iodine in food and drinking water. The author has carried on experiments in white rats to confirm other recent studies which call attention to the importance of positive goitrogenic factors. The experiments showed that goiter can be produced with regularity in white rats by a diet consisting of corn meal, rolled oats and calcium carbonate. The goitrogenic factor in this diet is the calcium ion. It was assumed from these experiments that in regions where the iodine content of the food is sufficient for a normal intake, goiter will develop if a powerful positive goitrogenic factor is present.

KAISER, Rochester, N. Y.

PSEUDO-HYPOPHYSECTOMY: A CONDITION RESEMBLING HYPOPHYSECTOMY PRODUCED BY MALNUTRITION. MICHAEL G. MULINOS and LEO POMERANTZ, J. Nutrition **19**:493 (May) 1940.

From a study of over 300 rats Mulinos and Pomerantz have obtained data on acute and chronic inanition and have compared the effects of those conditions with the tissue changes reported to occur after hypophysectomy. The changes in endocrine tissue are qualitatively similar in the two conditions but are seldom as marked in cases of inanition as they are after hypophysectomy. These authors believe that many of the effects of inanition are due to malnutrition of the hypophysis, resulting in a diminished secretion of hormones.

FREDEEN, Kansas City, Mo.

DIABETES MELLITUS IN CHILDHOOD AND ADOLESCENCE. TRACE D. CUTTLE, M. Clin. North America **23**:1515 (Nov.) 1939.

In several important particulars diabetes mellitus in the young differs from the disease in adults. The onset is abrupt and violent; the disease is more severe than it is in adults; it is usually progressive; it is more labile than it is in adults; there is more definite relation between juvenile diabetes and hyperfunction of the anterior lobe of the hypophysis than is the case in adults and the condition is not usually preceded by obesity or by degenerative changes.

In planning the treatment of the juvenile diabetic patient these peculiarities must be taken into consideration. The following standards should be fulfilled:

1. Adequate nourishment.
2. A level of blood sugar below 200 mg. per hundred cubic centimeters.
3. Less than 10 Gm. of dextrose in the urine in twenty-four hours.
4. A cholesterol content of the blood below 230 mg. per hundred cubic centimeters.
5. A normal psychologic adjustment and development.

The first four conditions are to be brought about by liberal diets without undue restriction of carbohydrates and the use of protamine zinc insulin in conjunction with unmodified insulin. The psychologic adjustment of the child to the limits imposed by the disease may present a difficult problem. He must be taught the nature of the disease which afflicts him, its dangers and his part in its control, while at the same time he is educated to live happily with his diabetes.

EUGENE H. SMITH, Ogden, Utah.

EFFECT OF INSULIN ON PLASMA LEVEL AND EXCRETION OF VITAMIN C. ELAINE P. RALLI and SOL SHERRY, Proc. Soc. Exper. Biol. & Med. **43**:669 (April) 1940.

Six normal dogs were found to excrete 20.6 mg. of vitamin C per kilogram of body weight in twenty-four hours, with fasting plasma levels of 0.55 to 0.94 mg. per hundred cubic centimeters, whereas 7 diabetic dogs given insulin excreted but 3.6 mg. in the same period, while the plasma levels varied from 0.33 to 0.71 mg. per hundred cubic centimeters. In both normal control and diabetic animals administration of insulin caused a decrease in the level of vitamin C in the plasma and in its excretion in the urine. Intravenous administration of dextrose overcame this effect of insulin on the urinary excretion and the level of vitamin C in the plasma.

HANSEN, Minneapolis.

EFFECT OF THYMECTOMY IN IMMATURE RATS. W. O. REINHARDT, Proc. Soc. Exper. Biol. & Med. **43**:732 (April) 1940.

Thymectomy and a control sham operation were performed on 46 rats 2 to 4 days old. The results revealed no significant effect on growth, development or

endocrine gland differentiation. These findings are in contrast to those reported when roentgen irradiation of the thymus is performed, in that the animals treated by irradiation are said to have a temporary arrest of development of the spermatogenic tissue of the testis. The authors believe that the mechanism of the effects produced by irradiation of the thymus region must be sought elsewhere than in the thymus gland.

HANSEN, Minneapolis.

RESPONSE OF VARIOUS BREEDS OF RABBITS TO HAMILTON AND SCHWARTZ TEST FOR PARATHYROID SECRETION. EMIL J. BAUMANN and D. B. SPRINSON, Proc. Soc. Exper. Biol. & Med. **44**:407 (June) 1940.

The authors observed that New Zealand white or chinchilla rabbits were less sensitive to parathyroid extract than were Dutch or Belgian breeds. They deem it advisable to determine the sensitivity of rabbits to be used for the Hamilton and Schwartz test. With this test, excessive circulating parathyroid hormone may be demonstrated by injecting blood into rabbits, administering calcium chloride by stomach tube and then determining the use of serum calcium in the animals. The animals should be at least 5 months old and should be kept on a diet which has a calcium-phosphorus ratio of 1 or more for several days.

HANSEN, Minneapolis.

THE END RESULTS OF THE SURGICAL TREATMENT OF THYREOTOXICOSIS. H. R. G. POATE and N. R. WYNDHAM, M. J. Australia **1**:505 (April 13) 1940.

From a study of 413 patients the authors conclude that:

1. In most cases of thyrotoxicosis (69.4 per cent) operation effects a perfect cure; in another 15.1 per cent the residual symptoms are mild.

2. Three common causes of imperfect health following operation are usually amenable to treatment, namely, hyperthyroidism, hypothyroidism and hypoparathyroidism.

3. Prolonged administration of iodine before operation militates against success. A long history of abnormality and cardiac impairment also make the prognosis worse.

4. Close cooperation between the physician and the surgeon is of benefit to both and also to the patient. A long period of observation is necessary after operation.

5. Approximately 60 per cent of thyrotoxic patients with auricular fibrillation may be restored to normal health.

6. The best anesthetic agent for operations on the thyroid has probably not yet been determined.

GONCE, Madison, Wis.

THE DIABETIC CHILD AND HIS TREATMENT. P. MAURIAC, Presse méd. **48**:65 (Jan. 17-20) 1940.

Diabetes in childhood is treacherous, unpredictable and often fatal, in spite of the advances made by the use of insulin. The patient, the parents and the physician must cooperate in a program which will be lifelong. As soon as the diagnosis is made, treatment must be started, as delay may be fatal. After a preliminary hospitalization for purposes of study and regulation, home care is preferable.

DAFFINEE, Boston.

A CASE OF CUSHING'S SYNDROME. A. GAREISO, S. SCHERE and J. C. PELLERANO, Arch. argent. de pediat. **12**:526 (Nov.) 1939.

The authors report a case of this rare condition in a girl 14 years old. She showed tremendous obesity of rapid evolution and of typical localization; hyper-

trichosis; genital symptoms, consisting of hypomenorrhea and amenorrhea; arterial hypertension; marked purpuric striations of the skin, and unusual fatigability.

The symptoms were all believed to be due to a basophilic adenoma of the anterior lobe of the hypophysis.

SCHLUTZ, Chicago.

Diseases of the Muscles, Bones, Joints and Lymph Glands

MUSCLE STRENGTH IN MYOTONIA ATROPHICA (DYSTROPHIA MYOTONICA) IMPROVED BY TESTOSTERONE PROPIONATE. FREDERICK H. HESSER, ORTHELLO R. LANGWORTHY and SAMUEL A. VEST, Endocrinology **26**:241 (Feb.) 1940.

These authors report on studies of 2 male patients, as follows: "Results of treatment were evident within the week of the first injection. Thereafter the grip became stronger rapidly, reached a peak within the next 2 weeks, and leveled subsequently at the higher baseline. Temporary withdrawal of the drug in one case was accompanied by decreased dynamometric values 4 days after the last injection. . . .

"Both patients were gratified with the outcome of treatment, especially by the sense of greatly increased strength and the general constitutional improvement. Buoyancy of spirit, feeling of well-being and lessened fatigability were noteworthy. Posture and gait improved noticeably. A weight gain of some 15 lb. occurred; this might have been due to hydration (retention of electrolytes, nitrogen and water), fat deposition (increased appetite), or actual muscle dimension changes (hypertrophy)."

JACOBSEN, Buffalo.

A STUDY OF JUVENILE GOUT IN A PATIENT SUFFERING FROM CHRONIC ERYTHRONOCLASTIC ANEMIA OF OBSCURE ORIGIN, TOGETHER WITH OBSERVATIONS ON THE PHYSICAL STATE OF URIC ACID IN THE BLOOD AND THE EFFECTS OF SPLENECTOMY. C. G. LAMBIE, M. J. Australia **1**:535 (April 20) 1940.

Lambie presents a case of chronic erythronoclastic anemia of a hitherto undifferentiated type dating from birth in an 18 year old boy and complicated by the onset of gout at the age of 14 years. The anemia, the gout and the effect of splenectomy on each of these conditions are discussed at length.

GONCE, Madison, Wis.

OSTEITIS FIBROSA DISSEMINATA. B. T. SHALLARD, M. J. Australia **1**:558 (April 20) 1940.

The author reports a case of osteitis fibrosa disseminata (cutaneous pigmentation in the form of brown nonelevated patches, premature sexual changes [in the female] and fibrocystic disease of bone) occurring in an 18 year old girl. At the age of 18 months the girl suffered from an illness which was diagnosed as acute anterior poliomyelitis. During this illness she was comatose for about thirty-six hours and her left arm became paralyzed. It was after her subsequent recovery that her parents first noticed the discoloration of the skin.

GONCE, Madison, Wis.

SYNDROME RESEMBLING TETANY WITH MUSCULAR HYPERTROPHY IN THE INFANT. L. RIBADEAU-DUMAS, J. CHABRUN, MARTROU and M. CHAMPAGNE, Bull. Soc. pédiat. de Paris **37**:257 (May) 1939.

An infant born after a difficult delivery showed signs of tetany at the age of 6 weeks. No improvement followed the usual treatment. The values for blood calcium, phosphorus and phosphatase were normal. Muscular hypertrophy, especially of the proximal parts of the extremities, was noted. The condition was considered neuropathic.

BENJAMIN, Montreal, Canada.

Diseases of the Eye

AMBLYOPIA. WALTER A. FORD, Wisconsin M. J. **39**:278 (April) 1940.

The author considers amblyopia a functional condition of subnormal vision without a demonstrable pathologic basis. It is not aided by corrective lenses. It is an acquired condition, and with proper management much can be done to correct it. It may occur in one or both eyes and is accompanied by squint in one third of the cases.

Amblyopia is a pediatric problem, and its early detection and treatment are most important in the prognosis. Routine tests of vision with charts for the illiterate should be made for all preschool children. The greatest cause for failure is that most patients when the condition is first recognized are beyond the age when the most efficient treatment can be given.

Therapy consists of several measures, chiefly correction of associated visual defects, strabismus, hyperopia, etc.; periods of occlusion for the good eye, and particularly orthoptic training, best done of course in an orthoptic clinic. The greatest difficulty is in securing the prolonged cooperation of both the child and the parents.

The author describes a series of 180 patients with amblyopia. Only 13 of these were brought for treatment between 3 and 5 years of age; 66 were observed under 12 years of age. Hyperopia and hyperopic astigmatism were present in 83.4 per cent of this group, myopic difficulties in 6.6 per cent and squint in 30 per cent.

JANNEY, Wauwatosa, Wis.

BUPHTHALMOS WITH FACIAL NAEVUS AND ALLIED CONDITIONS. A. J. BALLANTYNE, Brit. J. Ophth. **24**:65 (Feb.) 1940.

This paper contains the subsequent history of a case previously reported by the author in the *British Journal of Ophthalmology* (**14**:481, 1931). The patient is now a child 8 years of age. The appearance of the eye, which was trephined when the child was 3 weeks old, is unchanged. The trephine scar is ectatic and the lens completely opaque. There is perception of light but a doubtful field of projection. Extraction of the lens was attempted through an inferior section, but vitreous was lost, and later in the day an expulsive hemorrhage occurred, requiring enucleation of the eye. Histologic examination revealed a fairly extensive angioma of the choroid. As the facial nevus is congenital, it can be assumed that the choroidal lesion is also congenital. It may be sufficiently developed to establish the glaucomatous process during antenatal life (buphthalmos) while in others the evolution of the neoplasm is delayed until adult life, and then simple or secondary glaucoma results. This, broadly speaking, is the theory advanced by Ginsburg and by Hudelo.

The article contains one illustration. W. ZENTMAYER. [ARCH. OPHTH.]

MACULAR LESIONS IN THE YOUNG. E. REDSLOB, Ann. d'ocul. **176**:738 (Oct.) 1939.

Macular alteration in older persons is an everyday occurrence and is attributed to a wearing out of the retinal tissue from vascular disease. Bailliart pointed out that macular lesions in young persons are much less frequent and therefore less known. Most textbooks classify these cases as familial macular degeneration of the Stargardt or Behr type or as a complication of idiocy, such as the infantile type of Tay-Sachs or the juvenile type of Spielmeyer-Stock.

Characteristic points of such macular lesions are: (1) the familial and hereditary character, (2) an almost absolute analogy in the evolution of the disease, (3) bilaterality and (4) complete agreement between the subjective and the objective signs. Hereditary degenerations show themselves first between the sixth and eighth year, again at 14 and at 20 years and finally at old age, that is to say,

at the periods when the most manifest changes take place in the body development. In each family reported on by Behr the condition developed at the same ages—childhood, adolescence and old age.

The author has often observed hemorrhages in the macular area of young persons from 9 to 27 years of age. The cause of these is not known. They are encountered in persons who are otherwise perfectly normal but who present a certain fragility of the vessels. These hemorrhages are not destructive, do not cause much dimness of vision and do not provoke a central scotoma. They have been often observed in patients coming for examination of refraction. These lesions have no connection with the macular hereditary degeneration of Behr or with the cystic degeneration of Vogt.

S. H. McKee. [Arch. Ophth.]

Roentgen Therapy for Furuncles and Styes. L. Hambresin, Ann. d'ocul. **176**:803 (Nov.) 1939.

In the large majority of cases infection of the sebaceous glands of the lids recedes rapidly after treatment with moist, hot applications of slightly antiseptic fluid, which is sometimes assisted by a small incision or puncture with a fine galvanocautery. It is recognized, however, that there are cases also in which cure is difficult and takes place only after lengthy treatment. These conditions may also, in exceptional instances, be complicated by abscess of the orbit, phlebitis of the ophthalmic veins and thrombosis of the lateral sinus.

It is for this reason that the author brings forward a treatment which has been little used and with which his results have been satisfactory. He first gives a historical retrospect, then the technic of the treatment, the indications, contraindications, results and advantages. He believes that roentgen rays have given excellent results and suggests that perhaps they would be equally beneficial in cases of acute dacryocystitis, orbital periostosis and cellulitis of the orbit, at least in the early stages.

A bibliograpy accompanies the article.

S. H. McKee. [Arch. Ophth.]

Presentation of Photographs of Epicanthus. L. Babonneix, Bull. Soc. pédiat. de Paris **37**:273 (May) 1939.

Epicanthus is not necessarily associated with mongolism. It may be a familial trait. It may be explained on the basis of heredity as being linked to a gene.

Benjamin, Montreal, Canada.

Coloboma of the Optic Disk. A. Biffis, Ann. di ottal. e clin. ocul. **67**:522 (July) 1939.

A case of typical coloboma of the disk alone is described and illustrated. Areas of chorioretinal atrophy about the disk suggested the possibility that inflammation in utero at the time of development of the disk may have been responsible.

S. R. Gifford. [Arch. Ophth.]

Echinococcosis of the Orbit. R. R. Yarshavskaya, Vestnik oftal. **15**:82, 1939.

Two cases of echinococcosis of the orbit are reported. One case was that of a 17 year old student who had pain and bulging of the right eye for one month. There was marked exophthalmos, with edema and redness of the upper lid and papilledema of the fundus. A fistula was situated at the external canthus, with stringy matter discharging from it, which was found to be fragments of an echinococcus cyst. An incision after the method of Golovine was made, and the cyst was removed in fragments. Ten days later mastoiditis developed on the right side which necessitated anthrotomy.

The second patient, aged 24, had a gradually developing exophthalmos for one year with impairment of vision and hearing and a change in his mental behavior. The exophthalmos and papilledema were marked; a small tumor was palpated at the upper wall of the orbit. The left frontal lobe was involved, and the middle ear was inflamed. An echinococcus cyst with three small cysts included were found on operation. A few months later the mental symptoms disappeared, but the vision was poor because of atrophy of the optic disk.

The special features of these cases were: the formation of a fistula and the development of mastoiditis in the first case and involvement of the frontal lobe and otitis media in the second.

A detailed review of the literature is given. Of 191 cases reported from 1915 to 1937, 44 echinococcus cysts were reported in the Russian literature. Warshawskaya believes that Uhlenhuth's test of the blood should be done, as a positive reaction is specific for echinococcus cyst. O. Sitchevska. [Arch. Ophth.]

Skin Diseases; Allergy

Symposium on Allergic Dermatoses: Infantile Eczema. Rudolph Hecht, J. Allergy **11**:195 (Jan.) 1940.

Infantile eczema is not a well defined condition. Hill has subclassified the group into seborrheic dermatitis, contact dermatitis, eczematous fungous eruptions and atopic dermatitis. Any one or more of these may be present in the same person, and one form may be transformed into another. The differentiation of the various types from one another is sometimes impossible.

The diagnosis of infantile atopic dermatitis is based on a family history of atopy, the presence of immediate wheal type reactions to scratch or intracutaneous tests with the usual atopens, negative results to patch tests with contact substances, the presence of reagins in the serum and eosinophilia. Morphologically, there is an erythematous, papulourticarial, vesicular, frequently weeping eruption usually occurring on the face and neck and accompanied by violent uncontrollable itching.

Environmental substances, such as house dust and feathers, play a significant role in infantile eczema. The removal of these substances plus elimination of certain foods offer better results than just the elimination of certain foods. The best method of treatment is careful dermatologic management, including proper choice, application and removal of local remedies, bandages, careful splinting to prevent scratching, avoidance of soap, the use of sedatives and general hygienic and medical care. Mendelsohn, New York. [Arch. Dermat. et Syph.]

Metabolic Studies in Dermatomyositis, with a Note on the Effect of Wheat Germ. A. T. Milhorat, F. C. Weber and V. Toscani, Proc. Soc. Exper. Biol. & Med. **43**:470 (March) 1940.

Metabolic studies were made on 2 patients with dermatomyositis. The urinary excretion of calcium was found to be low and the phosphorus retention somewhat decreased; the magnesium balance was normal. The amounts of urinary creatinine were diminished in proportion to the amount of muscular wasting. Both patients had considerable creatinuria and impaired creatine tolerance. The patients were given 125 Gm. of wheat germ in tomato juice daily, and after two weeks there was a striking decrease in the creatinuria, with a slower rise in the creatinine excretion. At this time distinct clinical improvement was noted in these patients. Parenteral administration of riboflavin and administration of vitamin B_6 for six weeks were without effect. Hansen, Minneapolis.

BUTTER FAT IN DERMATITIS-PRODUCING DIETS. H. A. SCHNEIDER, Proc. Soc. Exper. Biol. & Med. **44**:266 (May) 1940.

Fresh butter fat fed at the 9 per cent level was able to prevent the occurrence of dermatitis in rats reared on a dermatitis-producing diet. Rats fed on a diet containing the same amount of fat which was rancid had dermatitis. Feeding with fresh butter cured the cutaneous lesions in these animals. Thus the antidermatitis action of fresh butter has been confirmed.

HANSEN, Minneapolis.

ETIOLOGY OF LICHEN URTICATUS OR STROPHULUS INFANTUM BASED ON 225 CASES. ERICH URBACH, Dermat. Ztschr. **78**:77 (July) 1938.

Hamburger and Dietrich reported unusual sensitivity to insect bites in children affected with lichen urticatus. They concluded that this factor was probably the determining one in the development of this disease. Urbach reaffirms his previous stand, pointing out that in 28 per cent of a series of 225 children with this condition hypersensitivity to certain foods could definitely be shown. Careful observations in the hospital eliminated the possibility of insect bites in a large group without beneficial effect. He admits that in some instances sensitiveness to external factors, such as wool and feathers, may play a part.

TAUSSIG, San Francisco. [ARCH. DERMAT. & SYPH.]

CLINICAL TRIAL OF VITAMIN B_6 IN CASES OF INFANTILE SEBORRHEA. W. PEHL, Ztschr. f. Kinderh. **61**:613 (Feb. 17) 1940.

In 6 of 8 cases the results were definitely negative; in the other 2 they were questionable. The vitamin was administered subcutaneously in 5 to 20 mg. doses (single or divided).

SIEMSEN, Chicago.

Miscellaneous

ACTION OF GASTRIC AND SALIVARY MUCIN ON PHAGOCYTOSIS. R. TUNNICLIFF, J. Infect. Dis. **66**:189 (March-April) 1940.

"Gastric and salivary mucin produce a covering on bacteria which prevents their staining vitally and inhibits their phagocytosis.

"In vivo experiments show that mucin-coated staphylococci are not taken up by leukocytes for two hours following injection, after which time they multiply enormously and kill mice in 24 hours. Control mice show phagocytosis of cocci at the end of one hour and recover.

"Vitally stained mucoid material in mice injected with mucin and staphylococci show unstained mucin-coated cocci as long as three hours after injection. Only stained cocci, uncoated with mucin, are taken up by the polymorphonuclear leukocytes."

AUTHOR'S SUMMARY.

DIAGNOSTIC ERRORS. SIEGFRIED WOLFF, Brit. J. Child. Dis. **37**:16 (Jan.-March) 1940.

This article consists of reports of 20 cases in which diagnostic errors were made but the correct diagnosis was established either clinically or at operation. The cases include 1 of diaphragmatic hernia; 12 in which the diagnosis of appendicitis either was made erroneously or was not made when it should have been made; 5 of tumor; 1 of intussusception, and 1 of congenital ranula.

In differentiating pneumonia and appendicitis the author emphasizes the value of examination of the urine. Absence of sodium chloride indicates pneumonia.

A case is cited to support the theory that acetonemic vomiting is due to anaphylactic shock. The striking and immediate relief obtained from a single injection of sodium phenobarbital in the presence of acetonemic vomiting is emphasized.

LANGMANN, New York.

Book Reviews

Diseases of Infancy and Childhood. Eleventh edition. By Emmett Holt, M.D., and John Howland, M.D.; revised by L. Emmett Holt Jr., M.D., and Rustin McIntosh, M.D. Price, $10.00. Pp. 1,421, with 262 illustrations. New York: D. Appleton-Century Company, Inc., 1940.

This book, which even in previous editions was a fine text on diseases of children, has been brought up to date. It has been largely rewritten and indubitably retains its place as one of the finest books in the field.

In accord with the growth of the field of pediatrics and the consequent impossibility for single authors to cover authoritatively all developments, Dr. Holt and Dr. McIntosh have adopted the method of symposium writing under their editorship. This edition is still the work of the editors of the previous ones, but they have had the collaboration of a large number of contributors who have special knowledge of single diseases or of particular phases of the broad field of pediatrics.

Dr. Holt and Dr. McIntosh have admirably edited their collaborators' contributions. They have succeeded in making the writing evenly paced. While keeping the advantages of the collaborators' accumulated knowledge, which is much wider than that which any single writer could offer, the book gives the impression that a single author was responsible for its writing. The editors have eliminated the decided disadvantages of duplication and variety of opinion which characterize many books by multiple authors.

Almost no subject is treated exactly the same as in previous editions. The discussion of some topics has been completely revised, and new chapters have been added. The sections on diseases of the blood, allergic disorders, congenital heart disease, psychopathologic problems, diseases of the newborn, nutrition, diseases of the bones and infectious diseases are vastly improved, the first three named being especially good. In general the topics are well covered. The greatest lack is the minimum of space allotted to the subjects of puberty and adolescence.

Most chapters include material which can be used by the practitioner, although that end seems to be secondary.

There are more illustrations than in the previous editions, and they are fairly good. Some are excellent, as are some of the charts. The reviewer, however, is still campaigning for more colored plates in textbooks.

The references and bibliography at the end of each chapter, as in previous editions, are good.

There probably is no better textbook for use in medical schools. Practitioners, also, will find it a fairly good reference book.

Growing Out of Babyhood. By William S. Sadler, M.D., and Lena K. Sadler, M.D. Price, $2.50. Pp. 344, with no tables or illustrations. New York: Funk & Wagnalls Company, 1940.

This book was written as "a handbook for parents on the problems of the preschool child." The authors have written rather extensively on habits of elimination, enuresis, nail biting, emotions and attitudes, thumb sucking, tantrums, feeding problems, discipline, sex problems, adjusting to the group and parent-child relationships.

Each subject is discussed from several points of view. Many methods for treating the same problems are sometimes given. A method for correcting thumb sucking is described thus: "First the thumb of the right hand is forcibly held in his mouth for one or two minutes and then, following a minute's rest, the thumb of the left hand is held in his mouth for a similar length of time, and so on for half an hour." Many other (fortunately less drastic) methods, as well, are sug-

gested. With respect to the treatment of enuresis, the authors state that "when one approach does not solve the problem, another must be faithfully tried," and "in certain aggravated cases, when other methods have failed, the sodium chloride treatment may be tried." Feeding problems are discussed from many angles, and several solutions are suggested. The underlying cause and significance of the problems are not discussed. The authors seem to describe all of the possible methods for outwitting the child into doing things, many of which he would do by himself if left alone—eating, for example.

Some of the medical ideas expressed are not generally accepted, such as, for example, that sleepwalking is a forerunner of "St. Vitus' dance." The language of the book is understandable to the laity. Interspersed with many helpful ideas for parents there are numerous confusing suggestions. Problems are discussed rather than the child. It is difficult to get the authors' conception of growth and their picture of normal childhood from reading the book.

Why Is the World Sick? By Dr. Paul K. Lipps. Price, $1.50. Pp. 136, with 13 illustrations. Boston: The Christopher Publishing House, 1940.

One of the temptations to be resisted in scientific research is the inclination to make a pet theory cover conditions to which it has little or no application, and the more far fetched the theory is the less the temptation seems to be resisted. An example is found in this book.

The book is purely theoretic, enlarging on the belief of the writer that all human illness is caused by animal parasites in the system: either directly, by irritative products of the parasites (cancer), or indirectly, by constipation, which results from the action of parasites on the intestinal wall (appendicitis).

Among the developments of the theory is the suggestion that a body which is weakened, presumably by parasitic action, cannot withstand changes in atmospheric pressure, with the result that sudden barometric shifts cause outward explosions of poisons lodged in the system.

The only experimental work cited is a list of the number of types of parasites found in the course of examinations made over fifteen years. This table shows, apparently, that examinations were made in a total of 5,200 cases, in 82 per cent of which parasites were found; but no case histories are given, and no evidence is submitted from these cases of parasitic infection in proof of the theory.

Outside of the lists of common parasites and the clear illustrations, which are those found in any text on parasitology, the book appears to this reviewer to have little merit beyond a certain entertainment value.

Expectant Motherhood. By Dr. Nicholson J. Eastman. Price, $1.25. Pp. 176, with 9 illustrations. Boston: Little, Brown & Company, 1940.

This publication is a complete and authoritative guidebook which merits the consideration of every physician in obstetric practice. It presents in a sane and reassuring manner the knowledge which the mother should have to promote intelligent cooperation with her physician. By presentation of the subject matter in a general rather than a specific, dogmatic manner the author nicely avoids the possibility that minor differences between his opinions and those of the individual physician will become an issue in the instructions to the patient. The selection of illustrations is excellent and reveals the author's effort to supply the information which is of the greatest interest to the mother. Explanation of routine procedures during pregnancy and labor familiarizes her with what she must expect and tends to prevent the apprehension so frequently encountered. In addition to answering many of the usual questions, which, though familiar to the physician, are entirely new and of great importance to the mother, the publication serves as an excellent liaison by providing a basis for more intelligent query on the part of the mother while permitting the maximum time and effort of the physician to be directed toward the specific instructions and explanations so necessary in the individual case.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
General Secretary: Dr. Kenneth D. Blackfan, 300 Longwood Ave., Boston.
Assistant Secretary-Treasurer: Dr. Charles F. McKhann, University of Michigan, Ann Arbor, Mich.

Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Place: Boston. Time: Postponed indefinitely.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

British Paediatric Association

President: Prof. Charles McNeil, 44 Heriot Row, Edinburgh, Scotland.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Nederlandsche Vereeniging voor Kindergeneeskunde

President: Prof. Dr. J. van Lookeren Campagne, Hofstraat 16, Gröningen, Holland.
Secretary: Dr. R. P. van de Kasteele, Laan van Poot 340, 's Gravenhage, Holland.
Place: Different places. Time: Three times a year.

Paediatrický Spolok na Slovensku

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASE IN CHILDREN

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

SOCIEDAD CUBANA DE PEDIATRÍA

President: Dr. Clemente Inclan Costa, Manrique 48, Habana.
Secretary: Dr. Serafin Falcon Lopez, Calle B No. 356, Vedado, Habana.
Place: Cátedra de Clinica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Jorge Muñoz Turnbull, Av. Alvaro Obregón 186, Mexico, D. F.
Secretary: Dr. Fernando López Clares, Medellín 191, Mexico, D. F.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincaré, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue du Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

URUGUAYAN SOCIETY OF PEDIATRICS

President: Dr. Conrado Pelfort, Av. 18 de Julio 1246, Montevideo.
Secretary: Dr. Héctor Mourigan, Av. 18 de Julio 2175, Montevideo.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. Julius H. Hess, 104 S. Michigan Ave., Chicago.
Secretary: Dr. Hugh L. Dwyer, 315 Alameda Rd., Kansas City, Mo.
Place: Cleveland. Time: June 2-6, 1941.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. J. B. Bilderback, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Statler Hotel, Boston. Time: Oct. 9-11, 1941.
Region I. Place: Hotel Taft, New Haven, Conn. Time: March 27-29, 1941.
Region II. Place: John Marshall Hotel, Richmond, Va. Time: April 24-25, 1941.
Region III. Place: Palmer House, Chicago. Time: May 15-17, 1941.
Region IV. Place: Fairmont Hotel, San Francisco. Time: May 1-3, 1941.

AMERICAN HOSPITAL ASSOCIATION, CHILDREN'S HOSPITAL SECTION

Chairman: Dr. D. L. Richardson, 593 Eddy St., Providence, R. I.
Secretary: Dr. Joelle C. Hiebert, 299 Main St., Lewiston, Maine.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Thomas B. Cooley, 1728 Seminole Ave., Detroit.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.
Place: Hot Springs, Va. Time: May 22-24, 1941.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. L. M. Lindsay, 815 Medical Arts Bldg., Montreal.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. A. Ashley Weech, 3975 Broadway, New York.
Secretary: Dr. Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia.

SECTIONAL

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Eugene Smith, 385–24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. R. Cannon Eley, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. James Marvin Baty, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. S. G. Henricke, 4215 N. E. Hancock St., Portland, Ore.
Secretary: Dr. J. S. Backstrand, 333 Wyatt Court, Salem, Ore.
Place: Doernbecker Hospital and University of Oregon Medical School, Portland. Time: Jan. 25, 1941.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. Donn Barber, 802½–8th Ave., Greeley, Colo.
Secretary: Dr. Kenneth Schmidt, Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7:30 p. m.

SOUTHERN MEDICAL ASSOCIATION, SECTION OF PEDIATRICS

Chairman: Dr. Harvey F. Garrison, 319 E. Capitol St., Jackson, Miss.
Secretary: Dr. Warren W. Quillian, 227 Aragon Ave., Coral Gables, Fla.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. M. V. Adams, 803 Government St., Mobile.
Secretary-Treasurer: Dr. William R. Britton, 4 Catoma St., Montgomery.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. William Belford, 233 A St., San Diego.
Secretary: Dr. John J. Miller Jr., 2398 Sacramento St., San Francisco.
Place: Del Monte. Time: May 1941.

FLORIDA STATE PEDIATRIC SOCIETY

President: Dr. Warren W. Quillian, 227 Aragon Ave., Coral Gables.
Secretary: Dr. George N. Leonard, 605 Lincoln Rd., Miami Beach.
Place: Concurrent with state association meeting at time of convention.

GEORGIA PEDIATRIC SOCIETY

President: Dr. R. C. McGahee, 1345 Greene St., Augusta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.

HEZEKIAH BEARDSLEY PEDIATRIC CLUB OF CONNECTICUT

President: Dr. D. C. Darrow, 789 Howard Ave., New Haven.
Secretary: Dr. Joseph L. Hetzel, 103 N. Main St., Waterbury.
Time: Three meetings a year.

ILLINOIS STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. Orville Barbour, 331 Fulton St., Peoria.
Secretary: Dr. Craig Butler, 715 Lake St., Oak Park.
Place: Chicago. Time: May 1941.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. K. T. Knode, 1105 E. Jefferson Blvd., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

IOWA PEDIATRIC SOCIETY

President: Dr. Morgan J. Foster, 837 Higley Bldg., Cedar Rapids.
Secretary-Treasurer: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. H. Aubrey White, Alexandria.
Secretary-Treasurer: Dr. W. C. Rivenbark, 3503 Prytania St., New York.
Place: Shreveport. Time: April 1941.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. Norman L. Hawkins, 11 Public Sq., Watertown, N. Y.
Secretary: Dr. William J. Orr, 135 Linwood Ave., Buffalo.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, PEDIATRIC SECTION

Chairman: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown.
Secretary: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Place: Pittsburgh. Time: Sept. 29-Oct. 2, 1941.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Harry Towsley, University of Michigan Hospital, Ann Arbor.
Secretary: Dr. Leon DeVel, 110 E. Fulton, Grand Rapids.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.
Place: Biloxi. Time: May 12, 1941.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. Herman M. Jahr, 1120 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. Elmer W. Bantin, 440 Aquila Court Bldg., Omaha.
Place: As announced by Committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NEW HAMPSHIRE PEDIATRIC SOCIETY

President: Dr. MacLean J. Gill, 14 N. State St., Concord.
Secretary-Treasurer: Dr. Ursula G. Sanders, 46 Pleasant St., Concord.
Time: Twice yearly.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Marion Y. Keith, 369 N. Elm St., Greensboro.
Secretary: Dr. G. W. Kutscher Jr., 176 Woodfin St., Asheville.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Ben H. Nicholson, 301 N.W. 12th St., Oklahoma City.
Secretary: Dr. Luvern Hays, 108 W. 6th St., Tulsa.
Place: Oklahoma Club. Time: 6:30 p. m., fourth Friday of each alternate month from September to May, inclusive.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. R. B. Josey, 1517 Hampton Ave., Columbia.
Secretary-Treasurer: Dr. Wilson Ball, South Carolina State Health Dept., Columbia.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Secretary: Dr. Gilbert Eblen, 611 W. Main Ave., Knoxville.

TEXAS PEDIATRIC SOCIETY

President: Dr. C. P. Jasperson, 509 Nixon Bldg., Corpus Christi.
Secretary-Treasurer: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Place: Fort Worth. Time: May 14, 1941.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. John M. Bishop, 511 Medical Arts Bldg., Roanoke.
Secretary: Dr. Edwin A. Harper, 301 Rivermont Ave., Lynchburg.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. Raymond Sloan, 1139–4th Ave., Huntington.
Secretary: Dr. Thomas G. Folsom, 1139–4th Ave., Huntington.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. D. Nourse, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. I. B. Silber, 10465 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. T. B. Verner, 170 St. George St., Toronto, Canada.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto, Canada.

BRONX PEDIATRIC SOCIETY

President: Dr. David Greene, 910 Grand Concourse, New York.
Secretary: Dr. F. E. Chick, 2325 University Ave., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. Archibald Smith, Garden City, N. Y.
Secretary: Dr. Walter Coles, 604–2d St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank van der Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places: Various cities in New York. Time: Third Tuesday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Philip Rosenblum, 2376 E. 71st St., Chicago.
Secretary: Dr. Bengt Hamilton, 826 E. 61st St., Chicago.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

DALLAS PEDIATRIC SOCIETY

President: Dr. Edgar Loomis, 351 W. Jefferson Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmont Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

DETROIT PEDIATRIC SOCIETY

President: Dr. Robert J. Mason, 460 Birmingham Rd., Birmingham, Mich.
Secretary: Dr. J. Hugh Lewis, 2966 Biddle Ave., Wyandotte, Mich.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

FULTON COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (ATLANTA, GA.)

Chairman: Dr. Stephen C. Redd, 157 Forrest Ave. N. E., Atlanta.
Secretary: Dr. C. Dixon Fowler, Medical Arts Bldg., Atlanta.
Place: Academy of Medicine, 38 Prescott St. N. E. Time: Second Thursday of each month from October to April, 8 p. m.

HOUSTON PEDIATRIC SOCIETY

President: Dr. Thomas J. Donovan, 3820 Fannin St., Houston, Texas.
Secretary: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

KANSAS CITY (MISSOURI) PEDIATRIC SOCIETY

President: Dr. John Aull, 1103 Grand Ave., Kansas City.
Secretary: Dr. George Herrman, 1107 Bryant Bldg., Kansas City.
Place: Kansas City General Hospital. Time: On call.

LOS ANGELES COUNTY MEDICAL ASSOCIATION, PEDIATRIC SECTION

President: Dr. Alonzo Cass, 1908 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Gladys Patric Shahovitch, 3936 Roderick Rd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

MEDICAL SOCIETY OF THE COUNTY OF KINGS AND THE ACADEMY OF MEDICINE OF BROOKLYN, PEDIATRIC SECTION

President: Dr. Sydney Nussbaum, 247 Ocean View Ave., Brooklyn.
Secretary: Dr. Harry Bikoff, 850 St. Marks Ave., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., second Monday of each month, October to March, inclusive.

MEDICAL SOCIETY OF THE COUNTY OF QUEENS, INC., SECTION ON PEDIATRICS

Chairman: Dr. A. A. Trivilino, 88-07–150th St., Jamaica, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144–38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION ON PEDIATRICS

President: Dr. Harry A. Ong, 1801 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. William F. Burdick, 5402 Connecticut Ave. N. W., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., fourth Thursday of every month.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. E. C. Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. R. P. Schowalter, 411 E. Mason St., Milwaukee.
Secretary-Treasurer: Dr. George H. Wegmann, 2650 W. Hopkins St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Chairman: Dr. Leslie O. Ashton, 850 Park Ave., New York.
Secretary: Dr. Alfred Langmann, 108 E. 68th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

NORTHERN CALIFORNIA AFFILIATES

President: Dr. Crawford Bost, 490 Post St., San Francisco.
Secretary: Dr. William A. Reilly, 384 Post St., San Francisco.
Time: Second Thursday of September, November, January, March and May.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. Harold Flanagan, 711 Lowry Medical Arts Bldg., St. Paul, Minn.
Secretary-Treasurer: Dr. Everett C. Perlman, 620 Medical Arts Bldg., Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

OKLAHOMA CITY PEDIATRIC SOCIETY

President: Dr. J. Byron Snow, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Place: Oklahoma Club. Time: Third Friday of each alternate month.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Pascal F. Lucchesi, 4000 N. Front St., Philadelphia.
Secretary: Dr. Aims C. McGuinness, Children's Hospital, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to April, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. E. L. Piper, 3200–5th Ave., Pittsburgh.
Secretary-Treasurer: Dr. Carl Ruder, 646 Washington Rd., Mount Lebanon, Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

RICHMOND PEDIATRIC SOCIETY

President: Dr. Charles L. Outland, 312 N. 9th St., Richmond, Va.
Secretary-Treasurer: Dr. T. Stanley Meade, 913 Floyd Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., third Thursday of each month, except June, July and August.

ROCHESTER PEDIATRIC SOCIETY

President: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Secretary: Dr. W. L. Bradford, 16 N. Goodman St., Rochester, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee. Time: Third Friday of each month from October to May.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Secretary-Treasurer: Dr. Peter G. Danis, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society Bldg. Time: First Friday of each month from October to June.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Jay I. Durand, 1305–4th Ave., Seattle.
Secretary: Dr. Frederick B. Joy, 1215–4th Ave., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Norman Nixon, 1136 W. 6th St., Los Angeles.
Secretary: Dr. Donald C. Shelby, 3780 Wilshire Blvd., Los Angeles.
Place: Jonathan Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Mark Osterlin, Central Michigan Children's Clinic, Traverse City, Mich.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (NEW YORK)

President: Dr. M. Bernard Brahdy, 531 E. Lincoln Ave., Mount Vernon.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Ave., Rye.
Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.